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VOL. I.—11TH YEAR.

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No. 6.

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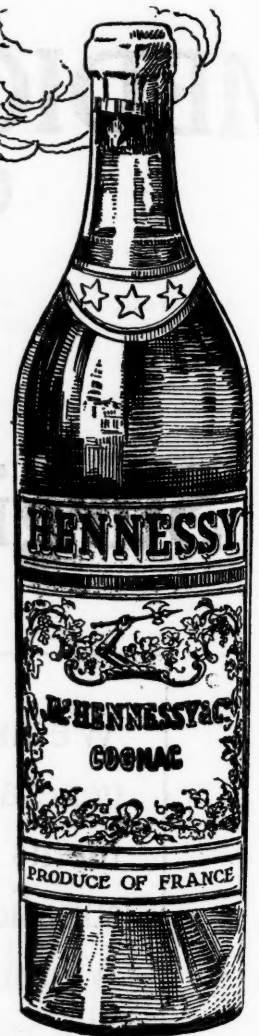
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### A STUDY OF THE INCIDENCE OF THE VARIOUS SEROLOGICAL TYPES OF PNEUMOCOCCI IN PNEUMONIA OF CHILDHOOD: OBSERVATIONS ON SERUM THERAPY.<sup>1</sup>

By REGINALD WEBSTER, M.D. (Melbourne),  
*Pathologist to the Children's  
Hospital, Melbourne.*

#### Introductory.

SINCE the almost synchronous reports of Dochez and Gillespie, of the Rockefeller Institute, and F. S. Lister, of the South African Institute for Medical Research, which appeared in 1913 and which clearly demonstrated that the immunity reactions of pneumococci provided a basis for the differentiation of these organisms into various distinct types, an immense amount of work has been carried out and a very extensive literature has accumulated on the subject of the relative frequency of occurrence of the several types of pneumococci in different countries.

Pioneer work in which the existence of serological differences amongst pneumococci was established, had previously been accomplished by Eyre and by

Neufeld, but it remained for the workers of the Rockefeller Institute to evolve the technique by which the infecting pneumococci could be recovered from pneumonic patients and identified with respect to "type" with sufficient rapidity to be of practically immediate use in the treatment and prognosis of pneumonia.

The searchlight thrown by this work on the hitherto irregular results attendant on serum therapy and the way pointed to a rational employment of specific serum treatment, were undoubtedly the principal factors in exciting a world-wide interest in the researches which have appeared in various numbers of the *Journal of Experimental Medicine* and in Monograph No. 7 of the Rockefeller Institute.<sup>(1)</sup>

#### Australian Work Hitherto Published.

As yet no very extensive investigations bearing on the serological varieties to be found among Australian pneumococci have been published. To the best of my knowledge the only observations recorded are those of Tebbutt,<sup>(2)(3)</sup> Penfold<sup>(4)</sup> and Paterson.<sup>(5)</sup>

The first mentioned dealt with a series of thirty-eight strains, nearly all of which were obtained from *post mortem* sources in the pneumonia of epidemic influenza. Type III. (eight) and Group IV. (nineteen) non-agglutinating pneumococci comprised

<sup>1</sup>Presented in abstract to the Section of Pathology and Bacteriology, Australasian Medical Congress (British Medical Association), first session, November, 1923, and published by permission of the Executive Committee.

twenty-seven out of thirty-eight strains examined and while these findings are of great interest as indicating under the conditions obtaining in epidemic influenza invasion of the lung by those pneumococci which are most frequently encountered in the air passages in health, they do not afford any information regarding the occurrence of the several types of pneumococci in lobar pneumonia as generally understood.

Penfold<sup>(4)</sup> shows the distribution of the different types of pneumococci in fifty-one strains examined at the Commonwealth Serum Laboratories as: Type I., 30%; Type II., 10%; Type III., 20%; an Australian type ("Setch"), 8%; and a heterogeneous group, 32%. He notes that the heterogeneous group in Australia is definitely larger than that obtaining in America.

Patterson<sup>(5)</sup> summarizes the observations at the Walter and Eliza Hall Institute of Research in Pathology and Medicine on the types of pneumococci present in one hundred and forty-seven instances of lobar pneumonia in adults. The figures given are Type I., 43%; Type II., 9.5%; Type III., 4.75%; heterogeneous group, 34.7%; streptococci, 8.1%.

#### Scope of Paper.

I am not aware of any work in Australia directed towards ascertaining the incidence of the various types of pneumococci in the pneumococcal infections of childhood and in this paper I propose to present a study in this field. I have restricted my attention to organisms of the pneumo-streptococcal group and have to report on two hundred and thirty-four cultures investigated as obtained from two hundred and twenty-three individual children.

#### Nomenclature.

It will be noted that the Australian workers above quoted have employed the American system of classification of pneumococci and throughout this paper pneumococci of Types I., II., and III. when so described are to be regarded as identical with those of the American Types I., II. and III. The Australian type "Setch" (Penfold) is designated as Type IV. and pneumococci inagglutinable by any of the sera at my disposal are referred to as belonging to the heterogeneous group.

#### Sources of Cultures.

In order that the work might be of immediate practical utility in providing the index for serum treatment by the rapid identification of infections due to Type I. pneumococcus, the sputum of children admitted to hospital suffering from lobar pneumonia was employed as the principal source of cultures. The examinations were limited as far as possible to children affected with lobar pneumonia for the reason that in this disease the specific aetiological factor is the pneumococcus, whereas broncho-pneumonia is not an entity in this sense. Any of a variety of bacteria among which are pneumococcus, streptococcus, *Bacillus influenzae* and *Staphylococcus aureus* may be encountered in the latter disease which, therefore, does not offer such a favourable prospect of gaining information regard-

ing the distribution of serological types of pneumococci as does lobar pneumonia.

It was found that the apparent difficulties in the way of obtaining sputum from young children can be almost invariably overcome. By the exercise of patience and persuasion many children of five or six years of age and upwards can be induced to cough and expectorate a specimen of sputum in the same manner as do adult patients. In very young children, however, the procedure adopted was to depress the tongue with a spatula and induce coughing by passing a swab over the tonsils and pharyngeal wall. The sputum could be observed as it was ejected from the glottis and was then caught on a clean swab or withdrawn between the swab and the end of the tongue depressor. The cotton wool swab, of pattern identical with that in everyday use for the transmission to the laboratory of material from infected throats, was then thoroughly rinsed in one to two cubic centimetres of sterile normal saline solution in a small vial; after the final step of expressing as much moisture as possible from the wool by pressure of the swab against the sides of the vial, the saline emulsion of sputum was ready for the inoculation of a mouse.

I wish to emphasize, however, the necessity of the bacteriologist obtaining the sputum himself when engaged in work of this nature among young children. He can never be certain that he has been provided with a genuine sample of muco-purulent bronchial secretion if its collection is left to nurses and during the whole course of this work I personally collected every sample of sputum employed.

Blood culture and lung puncture provide alternative methods of obtaining material for the isolation of pneumococci from children affected with pneumonia. The former is not always an easy procedure in young children and is attended by special difficulty in those of from two to five years of age in whom the fontanelle is closed and whose superficial veins are small. Even when the blood is obtained with facility, blood culture is by no means a reliable method of recovering the pneumococcus.

Lung puncture was employed in a few instances early in the course of the work, but was soon abandoned. While this method might be legitimately used when it is particularly difficult to obtain sputum or blood, it is open to certain objections. These may be stated as: (i.) the possibility of resultant pneumo- or hæmo- thorax, (ii.) the risk of infection of the pleural cavity, (iii.) the very great difficulty frequently experienced in localizing the pneumonic process by the data afforded by physical signs and the consequent lack of indication regarding the site of the proposed lung puncture.

Lister<sup>(6)</sup> who insisted on the use of blood culture or lung puncture, admitted that the performance of lung puncture was not always productive of a growth of the pneumococcus and reported an instance in which a brisk hæmoptysis was caused by lung puncture.

I am aware that the findings based on examination of the sputum in pneumonic patients may be questioned in respect to the aetiological significance of non-agglutinating pneumococci and streptococci



and propose to consider this point in a discussion of the heterogeneous group.

Other sources of cultures, as indicated in Table II., comprised pleural fluid, peritoneal and pericardial exudates, specimens of cerebro-spinal fluid and *post mortem* material.

#### Methods of Isolation.

The method adopted for the recovery of the pneumococcus was determined by the nature of the material to be examined.

In dealing with sputum the technique of mouse passage was followed almost exclusively. The mouse was also chosen for the isolation of pneumococci from *post mortem* material and in general whenever the specimen to be examined seemed likely to contain other bacteria along with the pneumococcus. At one period during 1922, when the supply of mice was temporarily short, I employed the benzidine-blood-agar medium elaborated by Penfold<sup>(7)</sup> and found it very useful.

The conspicuous advantage of the mouse method is, of course, its rapidity and whenever the number of mice seemed in danger of being inadequate to meet requirements, these animals were reserved for the determination of pneumococcus types from the sputum obtained from the children on their admission to hospital.

All specimens, such as pleural and arthritic exudates, in which an examination of a smear and a general consideration of their nature rendered it probable that they would yield a pneumococcus in a state of purity, were inoculated directly into broth.

In some specimens of cerebro-spinal fluid in which organisms were particularly abundant, it was possible to centrifugalize the bacteria down after a preliminary spinning to remove the cells. The overlying fluid was then decanted off and a saline emulsion prepared of the sedimented bacteria which, provided they conformed morphologically to pneumococci, were thus subjected to agglutination tests with the specific type sera.

Under circumstances which arose through the depletion of white mice much more rapidly than they were restored by breeding, I resorted to the ordinary brown mice (*Mus domesticus*) with entirely satisfactory results. Very efficient traps for catching these animals alive were placed in appropriate situations, notably in a hay and corn store, and I was enabled to maintain the work while the stock of white mice was replenished. I could detect no difference between the brown and white mice as regards their susceptibility to pneumococcus infection and proneness to die of pneumococcal septicaemia when inoculated with the sputum from a pneumonic patient.

The routine for the determination of pneumococcus types from sputum was as follows: The laboratory was notified of the admission to the medical wards of children in whom there had been made a provisional diagnosis of lobar pneumonia. At 4 p.m. each day I visited the medical wards and collected samples of sputum. Mice were usually inoculated at 5 p.m. and at 10 a.m. next day they would be found, as a rule, obviously ill or recently dead. Mouse autopsy was then performed and in

many instances it was possible to issue a report by mid-day. In those cases in which the peritoneal exudate of the mouse was not sufficiently rich in pneumococci or in which it showed a diversity of bacteria, determination of type was perforce delayed until the development of the culture from the animal's heart blood. Determinations made upon pneumococci recovered from the peritoneal washings were always confirmed by repeating the agglutination tests on a broth culture and the sheet anchor for the final determination of type was, whenever possible, a broth culture from the heart blood of the mouse.

In one hundred and thirty-one mouse autopsies pure cultures of pneumococcus were recovered from both peritoneum and heart blood in seventy-six instances; in forty-four cases the heart blood culture alone was pure and in eleven the peritoneal culture provided a pure growth, while that from the heart blood was sterile or contaminated.

Altogether the pneumococcus was cultivated in a condition of purity from the heart blood in one hundred and twenty instances as against eighty-seven pure cultures from the peritoneum.

In addition there were nineteen mice from which I failed to recover the pneumococcus from either source.

#### Broth Cultures.

Uniformly satisfactory results were obtained from the use of a plain veal broth in which the fundamental necessity was the accurate adjustment of the reaction to pH 7.8. Such a broth, as judged by the vigorous gas production which ensues when it is inoculated with *Bacillus coli*, contains a good deal of fermentable carbo-hydrate extracted from the veal. The reaction was adjusted by the colorimetric method with phenol-sulphone-phthalein as indicator and the need for care in this respect will be appreciated when it is realized, as shown by Avery and Cullen,<sup>(8)</sup> that growth of pneumococcus in broth containing fermentable carbo-hydrate ceases when a degree of acidity represented by pH 5.0 is reached.

Sterilization was effected by low pressure steam in a box sterilizer and no enrichment of the broth by the addition of serum or ascitic fluid was practised on account of the interference with the solution of pneumococci by bile so occasioned.

Broth cultures fulfilling the above conditions were ideal for the demonstration of bile solubility and for the performance of agglutination tests.

#### Criteria for Pneumococcus.

The close similarity which exists between pneumococci and streptococci, renders it necessary that rigid and authentic criteria should be observed in their differentiation and particular care is essential in the case of non-agglutinating cocci that they should be unequivocally demonstrated as pneumococci before being placed in the heterogeneous group.

As already indicated most of the strains reviewed in this paper were examined and identified in broth cultures and reliance was placed on the following characteristics for the distinction of pneumococci from streptococci.

The growth of the pneumococcus in broth produces a uniform haze or turbidity throughout the medium and frequently a fine dust-like deposit on the bottom of the tube. On the other hand very many streptococci but not all yield a growth which, by reason of the aggregation of the cocci into clumps, is not uniformly distributed throughout the medium, but which appears as flocculent masses.

These masses of bacteria may sediment and adhere to the sides of the tube to such an extent that the overlying medium is practically clear. The appearance is just that which would result from agglutination of a uniformly distributed culture; in fact, spontaneous agglutinability is a well recognized property of streptococci and has been an obstacle in the way of the differentiation of biological races among them by methods involving the use of agglutination tests.

Both pneumococci and streptococci form chains in fluid media, but the same difference as regards uniformity of distribution of the cocci is observed microscopically as has been indicated for the macroscopical appearances of broth cultures. The component cocci in the chains of a pneumococcal culture are more elongate than round, the chains are in general shorter and are evenly arranged in the field. The constituent cocci of a streptococcal chain are round, the chains are usually longer and the organisms are disposed in irregularly distributed clusters of intertwining chains.

The demonstration of hæmolytic power identifies an organism as a streptococcus as against a pneumococcus, but takes no cognizance of the large group of non-hæmolytic streptococci. In the course of this work advantage was taken of the frequently noted fact that the broth in routine use was isotonic to the extent that blood added thereto for the purpose of blood culture in the absence of growth of hæmolytic bacteria showed no hæmolysis at the end of forty-eight hours.

To five cubic centimetres of a culture in such broth 0.5 cubic centimetre of blood was added and

if no hæmolysis had occurred at the end of two hours, the organism was classed as non-hæmolytic.

The fundamental requisite for the recognition of a pneumococcus is that it should be soluble in bile. This phenomenon of bile lysis of pneumococci was first described by Neufeld and innumerable later observations have established the fact that bile solubility is a distinctive biological characteristic of the pneumococcus which separates it from closely allied organisms, such as the streptococcus.

In applying this test I used ox bile, a supply of which was obtained from the abattoirs every fourteen days. The bile was sterilized immediately on arrival and a quantity sufficient for the required tests filtered through paper each day just before use. The filtered bile was then added to the living broth culture in the proportion of one part of bile to five of culture.

In the case of pneumococcus cultures clarification was striking and unequivocal in the course of a few minutes.

The following table of strains from the laboratory notebook illustrates the manner in which the foregoing tests were applied in the identification of pneumo-streptococci.

It should be noted that not all the streptococci which failed in hæmolytic power, produced a green coloration in blood broth. I have, therefore, refrained from using the terms *Streptococcus viridans* and non-hæmolytic streptococcus as synonymous, as is the fairly frequent usage, and in the various tables have employed the general term non-hæmolytic streptococcus or *Streptococcus an-hæmolyticus*.

I made no use of carbo-hydrate fermentation as it is definitely stated in the monograph<sup>(1)</sup> that a study of a large number of strains of pneumococci embracing the several serological types failed to show any differences in bio-chemical reactions between members of distinct immunological groups.

A. L. Urquhart<sup>(2)</sup> came to the same conclusion.

TABLE I.

No.	Morphology.	Growth in Broth.	Hæmolysis.	Bile Solution.	Spontaneous Agglutination.	Organism.
14	Elongate coccus; chains of 8 to 10 evenly distributed	Diffuse haze	Nil	Complete	Nil	Pneumococcus
93	Rounded coccus; chains of 16 to 20 and upwards; irregularly distributed in field	Lumpy; flocculent; sedimented	Nil (green coloration)	Nil	+++	<i>Streptococcus viridans</i>
62	As above (93)	Granular appearance which returned after shaking into emulsion	Nil (no coloration)	Nil	+++	Streptococcus (non-hæmolytic)
99	Rounded coccus; long chains; fairly evenly	Whole of growth sedimented; supernatant broth clear	+++	Nil	+++	Hæmolytic streptococcus

The fermentation of inulin might have been employed to distinguish pneumococci from streptococci, but this at best is a very unsatisfactory test and failure of an organism to produce acid in inulin media would not weigh against the clear declaration of its nature as a pneumococcus afforded by solubility in bile.

#### Identification of Types of Pneumococci.

The separation of the pneumococci recovered into serological groups was effected by agglutination tests with specific agglutinating sera for Types I., II. and III. These sera were very kindly supplied me by Dr. A. B. Wadsworth, Director of the New York State Department of Health, and for the latter phases of the work I was furnished with serum for the recognition of the Australian type "Setch" (Type IV.) by Dr. W. J. Penfold.

Agglutination tests were carried out by the macroscopic technique on cultures of pneumococci in the simple veal broth above described and on emulsions of these organisms made with saline solution after centrifugalizing them out of the peritoneal washings from the mouse.

I did not attempt the precipitin reaction in the washing of the peritoneal exudate described by Blake,<sup>(10)</sup> as it requires a centrifuge of higher power than that with which I was provided to render the supernatant fluid water white.

A table of representative strains (see Table II.) illustrates the routine of agglutination tests, the serum dilutions employed and the agglutination titre of the several sera. Although the instructions furnished with the sera for Type II. and Type III. were that they should be used in dilutions of 1:2 and 1:5, I found that both sera agglutinated homologous organisms well in dilutions of 1:10 and incompletely in dilutions of 1:15.

The reaction in the lowest dilutions of all three sera (Type I., 1:10; Type II., 1:2; Type III., 1:2) was immediate and the increased turbidity which preceded the formation of clumps, was evident as soon as the serum

TABLE II.—To SHOW THE AGGLUTINATION TITRE RECORDED WITH HOMOLOGOUS ORGANISMS BY THE SPECIFIC DIAGNOSTIC SERA EMPLOYED.

No. of Culture.	Source.	Reaction with Bile.	Serum.												Normal Serum.		
			I.			II.			III.			IV.					
			1:10	1:20	1:40	1:60	1:2	1:5	1:10	1:15	1:2	1:5	1:10	1:15		1:20	1:40
5	Sputum	Soluble	+++	++	+	±	—	—	—	—	—	—	—	—	—	—	—
175	Arthritis	Soluble	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
122	Sputum	Soluble	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
221	Peritonitis	Soluble	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
73 <sup>1</sup>	Empyema	Soluble	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

<sup>1</sup> Heterogeneous.

and culture were brought into contact.

Throughout the work I was little troubled by cross-agglutination. The strains of pneumococci which behaved erratically with the type sera, were so few (five of one hundred and eighty-eight examined) that their aberrancies might be briefly indicated.

P70, P83, and P104 exhibited cross-agglutination in the lowest titres (1:2) of the sera of Types II. and III.

P49 agglutinated sluggishly and partially to the serum of Type III. in dilution of 1:5.

P65 gave a one plus (+) agglutination with the serum of Type II. in dilution of 1:2, but was unaffected by the 1:5 dilution.

After some hesitation as to whether the last mentioned should not be classed as a typical Type II., I placed all these organisms in the heterogeneous group.

#### Distribution of Types.

The aggregate figures for the two seasons, 1922 and 1923, are shown in Table III., in the compilation of which an endeavour has been made to indicate the relative frequency of occurrence of the several types of pneumococci and of streptococci in children affected with pneumonia or its complications, or pneumococcal process apart from pneumonia.

In Table IV. the percentage incidence of the various organisms is placed alongside that for a series of one hundred and forty-seven cases of lobar pneumonia in adults as determined by Dr. S. W. Patterson<sup>(5)</sup> at the Walter and Eliza Hall Institute of Research in Melbourne. Dr. Patterson's figures were published in July, 1922, and I presume were collected during 1921 and 1922.

Although in the examination of the sputum of children admitted as suffering from pneumonia an attempt was made to limit the investigation to lobar pneumonia, the disease in a certain proportion developed as broncho-pneumonia. The number (seventeen) is too few to warrant their consideration as a separate class, but the following table (Table V.) is

interesting as showing the relative infrequency of occurrence of the fixed types of pneumococci as determined by the examination of the sputum.

As regards the organisms recovered from sources other than the sputum in many instances in which the pneumo-streptococci were obtained from the purulent exudates of peritonitis, pericarditis, arthritis and meningitis, there was no antecedent pneumonia. The lobar or lobular character of pneumonia preceding the development of empyema is difficult of determination when the child comes to hospital with empyema established and for these reasons it is doubtful whether the figures obtained from a diversity of sources in children are comparable with those relating strictly to lobar pneumonia in adults.

If the seventeen examples of broncho-pneumonia above referred to be excluded and the findings in the adult series be compared with the results of the examination of the sputum in the lobar pneumonia of children, the figures more nearly approximate. When allowance is made for the fact that many of Dr. Patterson's cultures were obtained from *post mortem* sources, thereby excluding a number of doubtfully significant strains of the heterogeneous group, it can be fairly submitted that the incidence

of disease producing types of pneumococci in lobar pneumonia in children follows closely that observed in adults.

Table VII. is drawn up to show the distribution of the different types of pneumococci and of streptococci in relation to age-groups, as ascertained by examination of the sputum.

In the nine instances of infants under two years of age only one fixed type—Type II., was recovered. This, however, was perhaps the most interesting observation of the whole series as the baby, aged fifteen months, was admitted to hospital for the surgical treatment of purulent arthritis affecting the knee-joint. Pneumococcus Type II. was obtained from the pus evacuated from the joint and it was also isolated from the baby's throat. I subsequently demonstrated that the mother was a carrier of Type II. pneumococcus and as the observations on this mother and baby seem to be of such significance, I propose to make them the subject of a separate communication.

Table VIII. was compiled to show the difference in the percentage incidence of the serological types in the two seasons, 1922 and 1923.

TABLE III.—AGGREGATE FIGURES FOR 1922 AND 1923, TO SHOW THE RELATIVE FREQUENCY OF OCCURRENCE OF THE DIFFERENT TYPES OF PNEUMOCOCCI.

Source.	Pneumococci.					Streptococci.		<i>Staphylococcus aureus.</i>	Failures.
	I.	II.	III.	IV.	Heterogeneous.	Non-hæmolytic.	Hæmolytic.		
Sputum .. . . .	47	6	7	2	58	11	6	—	19
Empyema .. . . .	19	—	2	—	20	1	9	4	—
Cerebro-spinal Fluid .. . . .	1	—	—	—	8	1	1	—	—
Pericarditis .. . . .	1	—	—	—	2	—	—	—	—
Lung puncture .. . . .	1	—	—	—	1	3	—	—	6
Lung ( <i>post mortem</i> ) .. . . .	—	—	1	—	5	2	1	—	—
Peritonitis .. . . .	3	—	—	1	1	1	—	—	—
Arthritis .. . . .	—	1	—	—	—	2	2	—	—
Otitis .. . . .	—	—	1	—	—	—	2	—	—
Totals .. . . .	72	7	11	3 <sup>1</sup>	95	21	21	4	25
Percentage .. . . .	30.8	3	4.7	1.3	40.6	9	9	1.7	—

TABLE IV.—PERCENTAGE DISTRIBUTION.

Source.	Pneumococci.					Streptococcus.	<i>Staphylococcus aureus.</i>
	I.	II.	III.	IV.	Heterogeneous.		
Adults—lobar pneumonia— Melbourne Hospital .. . .	43	9.5	4.7	—	34.7	8.1	—
Children—all sources— Children's Hospital .. . .	30.8	3	4.7	1.3 <sup>1</sup>	40.6	18	1.7

<sup>1</sup> Limited number of strains examined.



By a coincidence it happened that the number of strains examined each year was the same (one hundred and seventeen). It will be seen that the percentage figure for Type I. pneumococci fell from 37.6 in 1922 to 23.9 in 1923, while there was a corresponding rise for the figure representing the heterogeneous group which is shown as 29% for 1922 and as 52.1% for 1923. This comparison applies to the pneumococci recovered from all sources in each year. The same variation as affecting Type I. pneumococci and those of the heterogeneous group is well shown in Table IX., in which the bacteriological findings in the pus evacuated from empyema are arranged separately for each year.

Thus, while in 1922 50% of empyemata were due to Type I. pneumococci, this particular race of pneumococcus was implicated in only 13% of the empyemata examined in 1923. In the latter season no less than 73.9% of empyemata were due to the activities of pneumococci of the heterogeneous group and hæmolytic streptococci.

Seasonal fluctuations in the distribution of the several types of pneumococci have been noted in other countries. The observation was made by the workers at the Rockefeller Institute for the United States and established for South Africa by Lister. In connexion with these seasonal variations it may be remarked that W. S. Thomas,<sup>(11)</sup> reviewing the experience of four and a half years at St. Luke's Hospital, New York, noted a complete absence of Type II. for a period of eighteen months during 1918-19. (The incidence of Type II. generally in the United States is placed in the region of 30%.) The same writer advances the view that pneumonia due to members of the heterogeneous group of pneumococci is endemic in the United States, but that Type I. lobar pneumonia is prone to occur in epidemic waves.

The incidence of the various biological races of pneumococci as causal agents in the production of lobar pneumonia varies in different countries, as will be seen from the following table which is

TABLE V.—BRONCHO-PNEUMONIA.

No.	Pneumococci.					Streptococci (non-hæmolytic).	Streptococci (hæmolytic).	Died.
	I.	II.	III.	IV.	Heterogeneous.			
17	1	—	—	1	9	4	2	3

TABLE VI.—TYPES OF PNEUMOCOCCI IN LOBAR PNEUMONIA OF CHILDREN AND ADULTS (PERCENTAGES).

Patients.	Number.	Pneumococci.					Streptococci.
		I.	II.	III.	IV.	Heterogeneous.	
Adults .. ..	147	43	9.5	4.7	—	34.7	8.1
Children— Children's Hospital, Melbourne ..	120	38.3	5	5.8	0.8 <sup>1</sup>	40.8	9.2

<sup>1</sup> Limited number of strains examined.

TABLE VII.—TYPES AS DISTRIBUTED IN AGE GROUPS.

Micro-Organisms.	Age Groups.						Totals.	
	2 Years and Under.		2—6 Years.		6—14 Years.			
	No.	Percentage for Group.	No.	Percentage for Group.	No.	Percentage for Group.	No.	%
Pneumococci—								
Type I. . . . .	0	0	24	38.0	23	35.4	47	34.3
Type II. . . . .	1	11.1	3	4.8	2	3.0	6	4.4
Type III. . . . .	0	0	2	3.2	5	7.7	7	5.1
Type IV. . . . .	0	0	2	3.2	0	0	2	1.5
Heterogenous Group . . . . .	7	77.8	26	41.2	25	38.5	58	42.3
Streptococci . . . . .	1	11.1	6	9.5	10	15.3	17	12.5
	9		63		65		137 <sup>1</sup>	

<sup>1</sup> One hundred and twenty patients with lobar pneumonia and seventeen with broncho-pneumonia.

TABLE VIII.

Source.	1922.										1923.										
	Pneumococci.					Streptococci.					Staphylo- coccus aureus.	Pneumococci.					Streptococci.				
	Hetero- geneous.				Non-hæmo- lytic.	Hæmo- lytic.	Staphylo- coccus aureus.	Hetero- geneous.				Non-hæmo- lytic.	Hæmo- lytic.								
	I.	II.	III.	IV.				I.	II.	III.				IV.							
Sputum .. .. .	23	4	4	—	20	11		5	—	24	2	3	2	38	1	1	—				
Empyema .. .. .	16	—	2	—	10	1	2	1	3	—	—	—	10	—	7	3					
Cerebro-Spinal Fluid .. .. .	1	—	—	—	2	—	—	—	—	—	—	—	6	1	1	—					
Pericarditis .. .. .	—	—	—	—	1	—	—	—	1	—	—	—	1	—	—	—					
Peritonitis .. .. .	3	—	—	—	1	—	—	—	—	—	—	1	—	1	—	—					
Lung Puncture .. .. .	1	—	—	—	—	3	—	—	—	—	—	—	1	—	—	—					
Lung (post mortem) .. .. .	—	—	—	—	—	2	1	—	—	—	1	—	5	—	—	—					
Arthritis and Otitis .. .. .	—	—	—	—	—	2	1	—	—	1	—	—	—	—	3	—					
Totals .. .. .	44	4	6	—	34	19	9	1	28	3	4	3	61	3	12	3					
Percentage .. .. .	37.6	3.4	5.1	—	29.0	16.2	7.7	0.8	23.9	2.6	3.4	2.6	52.1	2.6	10.2	2.6					

reproduced in order that the figures for Melbourne might be placed against them for comparison (see Table X.).

This table shows as its conspicuous feature the much greater frequency of occurrence of Type II. pneumococci in America and in England as compared with South Africa and Australia.

Sir Frederick Lister's figures for South Africa show the presence in that country of a large group (Group A=39%) which is not represented in America. A line of research which suggests itself for Australia, is that which might be directed towards ascertaining if our large heterogeneous group includes an Australian type of dimensions comparable with the American Type II.

The Australian Type IV. or "Setch" (Penfold) was found in this investigation on three occasions among forty-six strains subjected to agglutination tests with the appropriate serum.

The first two Type IV. cultures were derived from the sputum of two children affected with lobar and broncho-pneumonia respectively and the third pneumococcus of this type was obtained in pure culture from the purulent peritoneal exudate in a little girl upon whom laparotomy was performed for acute peritonitis. The peritonitis in this instance was of quasi-primary character. Fraser and McCartney<sup>(13)</sup> draw attention to the fact that "primary" pneumococcal peritonitis in children invariably affects girls and claim to have demonstrated the presence of pneumococci in the vagina under these circumstances. In this particular instance the finding of a specifically agglutinable pneumococcus in the peritoneal cavity created a good opportunity for identifying it or otherwise with any pneumococcus that might be recovered from the vagina, but two attempts to isolate pneumococci from the vaginal secretions failed.

#### The Heterogeneous Group.

Pneumococci of the heterogeneous group, when recovered from the sputum of children affected with pneumonia, must be treated with considerable reserve as regards their causal relationship to the disease. The same may be said of non-hæmolytic and even hæmolytic streptococci, as all these bacteria may be discovered in the throat apart from disease.

In the series under review opportunity for proof of the ætiological rôle of streptococci or non-agglutinating pneumococci isolated from the sputum of pneumonia patients arose very infrequently. Such

opportunity is afforded by development of a complication or by *post mortem* examination.

Of seventy-five children from whom non-agglutinating pneumococci or streptococci were obtained by examination of the sputum, sixty were affected with lobar pneumonia and fifteen with broncho-pneumonia. Two of the larger class and three of the smaller class (broncho-pneumonia) died. In one little girl whose sputum yielded a non-agglutinating pneumococcus (P.32), empyema and pericarditis supervened at a later stage. P.91, also a non-agglutinating pneumococcus, was recovered from the pus of the empyema.

The identity of two strains of the heterogeneous group one of which is recovered from the sputum early in the disease, and the other from a pathological exudate of later date or from the lung *post mortem*, can only be shown by the production of a monovalent agglutinating serum against one of them and determining if the other is susceptible to agglutination by such serum.

Observations on the agglutinating and opsonic capacity of the serum of the patient might also provide evidence that a given sputum pneumococcus of the heterogeneous group stood in causal relationship to the child's infection. To have attempted investigation along these lines would have rendered the work too complex for the time I was able to devote to it.

In several instances the sputum finding was subsequently shown not to have disclosed the pathogenic agent.

A non-haemolytic streptococcus, S.62, was isolated from the sputum of a child from whom the specimen was very difficult to obtain. Examination of a second and more satisfactory sample yielded pneumococcus Type I.

TABLE IX.—EMPYEMA.

Micro-Organisms.	1922.		1923.	
	No.	Per-centage.	No.	Per-centage.
Pneumococci—				
Type I. . . .	16	50	3	13
Type II. . . .	—	—	—	—
Type III. . . .	2	6.2	—	—
Type IV. . . .	—	—	—	—
Heterogeneous Group . . . .	10	31.2	10	43.5
Streptococci—				
Non-haemolytic . . . .	1	3.1	—	—
Haemolytic . . . .	2	6.2	7	30.4
<i>Staphylococcus aureus</i> . . . .	1	3.1	3	13
	32		23	

In another instance the non-haemolytic streptococcus, S.40, recovered from the first sample of sputum was discarded for a Type II. pneumococcus, P.41 obtained on a second attempt, while in each of two boys for whom a report of non-agglutinating pneumococcus was returned after examination of the sputum, empyema due to *Streptococcus haemolyticus* supervened.

Reference to Table III. shows that pneumococci of the heterogeneous group were obtained in relatively large numbers from situations in which their pathogenicity admitted of no question. The frequency of occurrence of the members of this group in empyemata during 1923 has already been noted; in nine instances of pneumococcal meningitis no less than eight of the infecting organisms were unclassifiable pneumococci.

Other members of this group were obtained from the exudate in two cases of pericarditis, one of peritonitis and on five occasions from the lung *post mortem*.

Non-agglutinating pneumococci were cultivated from sources other than sputum in twenty-six fatal infections and of sixty-three mice inoculated with sputum and subsequently yielding a pneumococcus of this character, thirty-eight were dead or in a moribund state within seventeen hours.

These facts are cited as evidence of the existence of many virulent strains among the unclassified pneumococci and as indicating the wide scope in Australia for work on the immunological reactions of this large group. The work is of such a nature however, that no hospital pathologist responsible for his share of routine diagnostic and *post mortem* work could possibly hope to carry it to a successful issue. It is a problem which demands the attention of a team of workers at a research institute. At a meeting of the Victorian Branch of the British Medical Association, held on June 7, 1922, Dr. W. J. Penfold communicated some results of studies undertaken at the Commonwealth Serum Laboratories and directed towards the subdivision of the unclassified pneumococci as they occur in Australia. His completed work will be of the greatest interest and importance.

It remains to consider the comparative severity of the infections in children due to the several types of pneumococci and manifesting themselves as lobar pneumonia.

Table XI. is designed to furnish the data upon which such comparison might be made, and also incorporates the figures which I obtained by an analysis of six hundred and twenty-six case records of lobar pneumonia occurring during 1921, 1922 and 1923. This number was reviewed in order to secure basic figures with which those relating to the different "types" and those for the serum treated might be compared. In this series of six hundred and twenty-six the type of pneumococcus was determined in one hundred and twenty only; the ages of the children ranged from two to fourteen years and none was treated with anti-pneumococcal serum.

The "type" cases considered are those in which the type was determined from the sputum at the time of the child's admission to hospital; obviously it is inadmissible in attempting to estimate incidence of complications and mortality rates to include those in which the only determination of type was made from the pus of an empyema or other complication or from *post mortem* material.

The accurate recording of the febrile period presented some difficulty in the large number of children who were ill for some days before they were brought to hospital, and in tabulating the number of days of fever it was assumed that the child was febrile from the day he became ill.

From Table XI. it appears that the figures for lobar pneumonia due to Type I. pneumococcus exceed the average as given in the first row in respect to febrile period, stay in hospital and incidence of complications. The group in which non-agglutinating pneumococci were recovered from the sputum, comprises forty-nine examples of lobar pneumonia which on the average were milder than the standard indicated by the first line in the table, and definitely less severe than the Type I. infections.

Witness the 10.2% of complications in general and 4% of empyemata in the heterogeneous group as compared with 17% and 10.6% respectively in the Type I. group.

The incidence of empyema in the forty-seven cases of Type I. lobar pneumonia (10.6%) is greater than that recorded for the six hundred and twenty-six of all varieties in the great majority of which the type was undetermined. In this much larger series empyema occurred in thirty-nine or 6.2% of the children represented.

The suggestion offered by these findings is that there is special liability to involvement of the pleura in Type I. infections and if the table of the bacteriological findings in empyema be examined (Table IX.) the figures for 1922 support the proposition.

In 1922 50% of empyemata were due to pneumococcus Type I., but the predominance of non-agglutinating pneumococci and streptococci and the minor position occupied by Type I. pneumococcus (13%) in the empyemata of 1923 seem to point to its leading position in the former year as having been a seasonal phenomenon.

TABLE X.

Group or Type.	Country.				
	United States of America.	South Africa.	England.	Victoria (Melbourne).	
				Walter and Eliza Hall Institute.	Children's Hospital.
Type I. . . . .	33%	—	30.6%	43%	38.3%
= Group C . . . . .	—	20%	—	—	—
Type II. . . . .	29%	—	32.7%	9.5%	5%
= Group B . . . . .	—	11%	—	—	—
Type III. . . . .	13%	—	6.7%	4.7%	5.8%
= Group E . . . . .	—	2%	—	—	—
Heterogeneous—Group IV. . . . .	20%	—	30%	34.7%	40.8%
Group A . . . . .	—	39%	—	—	—
Group D . . . . .	—	6%	—	—	—
= Group F . . . . .	—	8%	—	—	—
Group G . . . . .	—	4%	—	—	—
Group X . . . . .	—	6%	—	—	—
Unclassified . . . . .	0	4%	0	0	0
Type II.—Atypical. . . . .	5%	—	0	0	0

TABLE XI.

Type of Pneumococci.	Total Number of Patients.	Average Duration of Fever (Days).	Average Stay in Hospital (Days).	Complications.		Deaths. Number.	Mortality in Adults. <sup>2</sup>	
				Number.	Empyema. Number.		Number.	Percentage of Deaths.
	626	9	11.1	71=11.3%	42= 6.7%	39=6.2%		
Type I. . . . .	47 <sup>1</sup>	9.8	13.2	8=17%	5=10.6%	1=2.1%	63	33.3
Type II. . . . .	6	11	15.5	—	—	—	14	14.3
Type III. . . . .	7	12.1	16.1	2	—	—	7	14.3
Heterogenous Group . . . . .	49	8.5	11.3	5=10.2%	2= 4.0%	2=4.0%	57	37.2

<sup>1</sup> Including fifteen treated with serum.<sup>2</sup> According to Patterson.<sup>(6)</sup>



It is to be noted, however, that Lyon<sup>(14)</sup> encountered pneumococcus Type I. in 72% of thirty-two cases of post-pneumonic empyema in children studied by him and found that in thirty-two instances of pneumonia charged to this type, empyema occurred twelve times, a percentage frequency of 37.8.

This, however, may have been seasonal and local, for among twenty-three examples of Type I. lobar pneumonia in Melbourne in 1922 empyema occurred three times (13%) and in twenty-four instances of lobar pneumonia due to Type I. pneumococcus in 1923 there were two empyemata (8.3%).

#### Serum Treatment.

I now enter upon the consideration of a subject which has given rise to much discussion at the Children's Hospital, Melbourne, and in regard to which I have made an earnest attempt to collect reliable data upon which a sound conclusion as to the efficacy of serum treatment in the lobar pneumonia of childhood might be based.

It must be admitted at the outset, however, that as the result of the routine identification of types of infecting pneumococci during two winter seasons in order that Type I. infections might be selected for serum treatment, the information gained is somewhat meagre and the number of children adequately treated with serum is small.

For adequate specific therapy not only is it necessary to administer a sufficient dose of serum, but it is of equal importance that the serum should be given in the early stages of the disease. The second condition was not always fulfilled, as some children to whom serum was given, had been ill for a week before they were brought to hospital.

Again, serum was not given to those children who were very mildly ill and who had, perhaps, reached the fourth or fifth day of the disease before they were identified with respect to type, as it was not considered that such clinical types afforded good opportunities for estimating the effects of serum therapy. In the generally favourable course pursued by lobar pneumonia in childhood the crisis was due to occur in these children at any time and it was felt that a fall in temperature might have

been connected with an injection of serum in many instances in which it was merely coincident.

At the same time selection was not carried to the extent of reserving specific therapy for the desperately ill and in general if a child was admitted in the first days of the disease, exhibited a considerable degree of intoxication and was shown to be infected with Type I. pneumococcus, he was considered an appropriate subject for serum treatment.

The number of children who received serum treatment was fifteen.

Table XII. is compiled from data which may serve to estimate the clinical results in a series of patients affected with lobar pneumonia, in all of whom the infecting pneumococcus was demonstrated as Type I. and all of whom received monovalent Type I. anti-pneumococcus serum.

The average figures for lobar pneumonia generally as well as those for a number of Type I. children to whom no serum was given are included.

The table also includes the figures relating to a series of thirty children who during 1920 and 1921 before I was in a position to identify the types of pneumococci, were treated by the administration of polyvalent anti-pneumococcus serum.

If Table XII. demonstrates anything, it is the difficulty of attempting to draw conclusions from a relatively small number of observations. At the same time a large collection of examples of Type I. lobar pneumonia composed of children for whom serum therapy seemed appropriate could only be accumulated over a series of years.

From the table it appears that there is little to choose between the results obtained in the Type I. children who were given the benefit of specific monovalent serum therapy, and those who, identical bacteriologically, were not so treated. Table XII., however, needs to be considered in conjunction with Table XIII.

There were no deaths among the fifteen serum-treated patients, but before the fact that one death occurred in the group of thirty-two in which no serum was employed, is set against this, it must be pointed out that the fatality happened in the twenty-sixth child of the series. In other words

TABLE XII.

Patients.	Number.	Average Duration of Fever (Days)	Average Stay in Hospital (Days).	Complications.	Mortality.	
					Number of Deaths.	Percentage.
Serum-treated—Type I. ..	15	7.8	12.9	Empyema .. } Nephritis .. } 3=20% Pneumothorax }	0	—
No serum given—Type I. ..	32	10.5	13.2	Empyema .. 4 } Nephritis .. 1 } 5=15.6%	1	3.1
Treated with polyvalent serum irrespective of type	30	10.9	17.9	Empyema .. 1 } Colitis .. 1 } 5=16.6% Otitis .. 3 }	0	—
Basic figures .. . . .	626	9	11.1	71=11.3%	39	6.2

there were twenty-five consecutive children with Type I. lobar pneumonia, untreated by serum, among whom no death occurred.

Similarly, although thirty children are shown as treated with polyvalent serum with no mortality, it is not a difficult matter to find in the tables compiled for the analysis of the six hundred and twenty-six case records which provide the basic figures, a consecutive series of thirty for whom no serum therapy was employed and among whom no death occurred.

It is noteworthy that the febrile period in the first group in the table, which is composed of serum-treated Type I. children, is appreciably less than that in any of the other three groups.

The figure for the percentage incidence of complication in the Type I. serum-treated patients is higher than that for any of the other three groups, but unqualified it does not convey a fair impression.

The boy in whom the empyema developed, was given an inadequate dose of serum (forty cubic centimetres) at the late stage represented by the seventh day of the disease. Pus was obtained by exploration on the tenth day.

The nephritis recorded for another boy was very mild and the evidence thereof had disappeared when he left hospital on the eleventh day.

Pneumothorax is noted in another child. Serum (forty cubic centimetres) was not given to this boy until the tenth day and therefore cannot be said to have had a fair chance of influencing the course of the disease.

It is necessary, therefore, to subdivide the serum-treated Type I. group in order that those patients who received the monovalent serum early in the course of the disease, should be considered apart from those to whom it was given at a comparatively late stage. I have selected the fifth day as demarcating the two classes and find that seven patients received anti-pneumococcal serum (Type I.) not later than the fifth day. The average febrile period for these seven was 4.7 days and the duration of their stay in hospital averaged 8.8 days. The only complication was that of a mild degree of nephritis to which reference has already been made. In five of the seven the temperature fell by crisis during the twenty-four hours immediately following the injection of the serum, which was made on the second day in one instance, on the fourth day in

three and on the fifth day in the remaining three. The average amount of serum given was one hundred and fourteen cubic centimetres.

Table XIII. give a comparison of results obtained in Type I. lobar pneumonia when serum was administered on or before the fifth day, with those of the Type I. series in which no serum treatment was employed.

Unfortunately the number of children whose infection was of the appropriate type and who received a sufficient dose of serum early in the disease, is not large enough to warrant anything of the nature of a general statement regarding the therapeutic efficacy of the Type I. anti-serum, but it may be said that in five of the seven a dramatic change in the child's clinical condition followed immediately on the injection of the serum. In the other two the injection was repeated and the crisis followed the second dose.

One boy, No. 146, was particularly ill, cyanotic and wildly delirious for two days preceding the injection of Type I. serum intravenously; on the following morning the temperature was normal and the boy was quiet and comfortable.

Thus, for the reasons already detailed I have been compelled to limit the discussion of experience in the serum therapy of lobar pneumonia at the Children's Hospital, Melbourne, to the consideration of a few individual instances rather than attempt the presentation of conclusions based upon statistical data. From clinical observation, however, it appears to me permissible to state the position thus: In the majority of children there appears to be no clinical necessity for serum treatment. By comparison with adults the outlook in lobar pneumonia in children is good and the young patients do not, as a rule, exhibit the serious toxæmia so frequently occasioned by this disease in older persons. At the same time individual instances arise among children which call for active, rather than expectant measures, and in such, if a Type I. infection be demonstrated, an intravenous injection of fifty cubic centimetres of the monovalent serum should be given and repeated if the chart records no improvement within twenty-four hours.

It is outside the scope of this paper to deal with the technique of serum administration, the preliminary tests for sensitiveness and the measures to be taken for desensitization. These questions are

TABLE XIII.

Treatment.	Number.	Average Duration of Fever (Days).	Average Stay in Hospital (Days).	Complications.	Mortality.
Serum given on or before fifth day . . . . .	7	4.7	8.8	Nephritis . . . .	—
No serum given . . . . .	32	10.5	13.2	Empyema . . . . 4 } Nephritis . . . . 1 } 5	1 = 3.1%
Basic figures . . . . .	626	9	11.1	71	6.2%

exhaustively discussed in readily accessible medical literature.

I am under great obligation to Dr. A. B. Wadsworth, Director of the New York State Department of Health; Dr. W. J. Penfold, Director of the Commonwealth Serum Laboratories; Professor T. Brailsford Robertson, of the University of Adelaide; and Dr. S. W. Patterson, until recently in charge of the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne, to each of whom I have applied at different times for help, either in materials or advice.

#### Summary.

A study to determine the relative frequency of occurrence of the several types of pneumococci in lobar pneumonia and other pneumococcal infections of childhood is presented.

The distribution of types of pneumococci in lobar pneumonia in children follows closely that observed for adults in the same centre.

While Type I. pneumococci occur in Australia with about the same frequency as in England and America, the Type II. group is very small in this country and the heterogeneous group correspondingly large.

Many highly pathogenic strains were found to belong to the heterogeneous group.

The Australian Type IV. was identified three times among forty-six strains examined.

Striking seasonal variations in regard to the incidence of Type I. pneumococcus is demonstrated.

The differentiation between pneumococci and streptococci and agglutination tests on the former are very satisfactorily carried out in broth cultures.

Routine serum treatment is not necessary in lobar pneumonia of childhood, but in seven selected children to whom monovalent Type I. serum was administered early in the disease, the crisis occurred within twenty-four hours of the injection of the serum in five and followed immediately on a second injection of serum in the other two.

#### References.

- <sup>(1)</sup> O. T. Avery, A. M. Chickering, R. Cole and A. R. Dochez: "Acute Lobar Pneumonia: Prevention and Serum Treatment," Monograph No. 7, of the Rockefeller Institute for Medical Research, October, 1917.
- <sup>(2)</sup> A. H. Tebbutt: "The Bacteriology of Influenzal Pneumonia," *THE MEDICAL JOURNAL OF AUSTRALIA*, December 13, 1919, page 499.
- <sup>(3)</sup> A. H. Tebbutt: "On Pneumococci in Pneumonia in Sydney," *THE MEDICAL JOURNAL OF AUSTRALIA*, March 19, 1921, page 228.
- <sup>(4)</sup> W. J. Penfold: "Developments in the Production of Therapeutic Sera of Australia," *THE MEDICAL JOURNAL OF AUSTRALIA*, March 26, 1921, page 245.
- <sup>(5)</sup> S. W. Patterson: "The Prognosis of Lobar Pneumonia and the Influence of Serum in Treatment," *THE MEDICAL JOURNAL OF AUSTRALIA*, July 29, 1922, page 115.
- <sup>(6)</sup> F. S. Lister: "Specific Serological Reactions with Pneumococci from Different Sources," Publications of the South African Institute for Medical Research, No. II., December 22, 1913.
- <sup>(7)</sup> W. J. Penfold: "The Action of the Pneumococcus on Aromatic Amino-Bodies," *THE MEDICAL JOURNAL OF AUSTRALIA*, July 29, 1922, page 120.
- <sup>(8)</sup> O. T. Avery and G. Cullen: "Hydrogen Ion Concentration of Cultures of Pneumococci of the Different Types in Carbo-Hydrate Media," *The Journal of Experimental Medicine*, 1919, Volume XXX., page 359.
- <sup>(9)</sup> A. L. Urquhart: "Serological and Morphological Characteristics of the Pneumococcus," *The Journal of the Royal Army Medical Corps*, 1922, Volume XXVIII., page 171.
- <sup>(10)</sup> F. G. Blake: "Methods for the Determination of the Pneumococcus Types," *The Journal of Experimental Medicine*, 1917, Volume XXVI., page 67.
- <sup>(11)</sup> W. S. Thomas: "Type I. Pneumococcus and its Serum Treatment," *The Journal of the American Medical Association*, December 31, 1921, page 2101.
- <sup>(12)</sup> F. Griffith: Reports on Public Health and Medical Subject, No. 13, Ministry of Health, 1922.
- <sup>(13)</sup> J. Fraser and J. E. McCartney: "Pneumococcal Peritonitis," *The British Journal of Surgery*, 1921-1922, Volume IX., page 479.
- <sup>(14)</sup> A. B. Lyon: "Bacteriologic Studies of One Hundred and Sixty-five Cases of Pneumonia and Post-Pneumonic Empyema in Infants and Children," *The American Journal of Children's Diseases*, January, 1922, page 72.
- <sup>(15)</sup> F. S. Lister: Quoted by Tebbutt.<sup>(12)</sup>

### Reports of Cases.

#### GUMMA OF THE SPINOUS AND TRANSVERSE PROCESSES OF THE FIRST THORACIC VERTEBRA.

By T. A. B. HARRIS, M.B., B.S. (Melbourne),  
Ipswich Hospital, Queensland.

P.B., a male, aged thirty-six years, a boilermaker's assistant, was first seen in the out-patient's department on April 3, 1923. He complained that for the past eight weeks he had had intense pain over the upper part of the chest, shooting down both arms. The pain was becoming progressively worse and for the past three weeks his neck had been stiff and painful.

He carried his head bent well forward and held stiff in the middle line with his back hunched. Rotation from side to side was possible, while flexion, extension and lateral flexion was very painful and almost impossible. He was a big, husky fellow of eighty-two and a half kilograms (thirteen stone). He had had no previous illness. His wife had four healthy children; she had had one miscarriage and was in good health. He had lost no weight; his appetite was good and he had had no night sweats. On examination of his heart, lungs and abdomen nothing abnormal was detected. There was a definite kyphosis with its apex at the spine of the first thoracic vertebra, where also there was a well defined lump continuous and around the spine of the first thoracic vertebra with no fluctuation. On the anterior surface of the chest wall epicritic sensation was impaired along the distribution of the first and second thoracic nerves. This loss of sensation became more marked in the area of distribution of the eighth cervical and first thoracic nerves from the upper part of the arm towards the fingers. The little fingers were quite anaesthetic, knee jerks, biceps jerks and plantar reflexes were normal. The eyes reacted to light and accommodation and the pupils were equal in size. There was no pain on jarring the vertebral column, but the spine and lateral processes of the first thoracic vertebra were very tender on palpation.

No focus or any suggestion of malignancy was detected. He was admitted and given sodium salicylate (1.2 grammes) three times a day and his head and neck were controlled between sand bags. A von Pirquet test was made, but no reaction was obtained. A skiagram revealed an area of rarefaction in the arch of the first thoracic vertebra with a hazy outline in the transverse processes of this and the eighth cervical vertebra. He received no relief from the sodium salicylate. The general examination together with the X-ray plates and excruciating nature of the pain made the condition appear to be a tumour, extradural in nature. A malignant tumour, spondylitis and tuberculosis did not fit into the picture and on April 9 a blood specimen was sent for a Wassermann test. The result was reported as a "++++" reaction. This, although



it did not exclude hydatid, made the diagnosis of gumma probable. He was given a mixture of mercury and iodide of potash and was given weekly injections of one cubic centimetre of grey oil intra-muscularly for ten injections. "Nov-arseno-billon" was given intravenously once a week starting with 0.15 gramme, then two injections of 0.3 gramme and ten injections of 0.6 gramme. He was discharged to out-patients on May 19, 1923, and had by July 7 finished his course of injections. By this time the lump over the first thoracic vertebra had disappeared, his neck was straight, his pain had gone and he had free movement of his neck in all directions. On July 24 a Wassermann test was carried out, but no reaction was obtained.

He was by this time well enough to return to work and his treatment for the next three months consisted of *pulvis hydrargyri cum creta*. On November 3 his serum again failed to react in the Wassermann test and in spite of his work he had no return of pain or disability.

This case seems interesting from the point of view of prognosis and also from, I believe, the rare situation of a gumma.

#### EXTENSIVE SLOUGHING DURING LABOUR.

By H. A. RIDLER, M.B., Ch.M. (Sydney).

Honorary Assistant Surgeon, Royal Hospital for Women, Sydney.

THE following report is of interest on account of the extensive sloughing caused by the length of labour.

Mrs. A.B., a primipara, aged twenty-three years, was admitted to the Royal Hospital for Women, Sydney, on January 15, 1923, with a history of having been in labour for eight days. On admission her temperature was normal, her pulse rate was one hundred and thirty-six and her respirations numbered thirty-six in the minute. The abdomen was enormously distended and resonant on percussion. In consequence the patient was very restless. At the vulva a large *caput* was projecting for some distance and could not be pushed up. The head was perforated and crushed and with great difficulty a large and swollen infant was delivered. During this procedure a large quantity of offensive gas escaped from the uterus. After the delivery of the infant no *fundus uteri* could be felt. A hand was therefore inserted into the uterus; the placenta was found lying free and was removed. A careful examination was then made of the walls of the uterus to make sure that there was no rupture. None was found. The sensation conveyed to the examining hand in the large and thin-walled uterus was very strange when compared to the normal uterus after delivery. An intra-uterine douche was given and one cubic centimetre of "Pituitrin" was injected every four hours. No *post partum* hæmorrhage occurred. The patient was desperately ill for some weeks. The temperature did not maintain a normal level for twenty-four hours until February 27, 1923. The sloughing of the soft parts on account of the prolonged pressure was very extensive. There is a recto-vesico-vaginal fistula. The bladder wall in the region of the trigone and close to the ureteric orifices is missing. The entire cervix is absent and the opening into the rectum is extensive, part of the external sphincter muscle is missing. An attempt is to be made to repair these fistulae. The size of the patient's pelvis was normal. The dystochia was evidently due to the size of the infant. It would appear that the gas originated from the fœtus.

#### Reviews.

##### THE AUSTRALIAN AIRMEN IN WARFARE.

Volume VIII. of the official history of Australia in the War of 1914-1918 deals with the activities of the Australian Flying Corps. F. M. Cutlack has woven a highly inter-

esting and often exciting chronicle of this *corps d'élite* from its modest beginning in the early months of 1915 to the end of the war.<sup>1</sup>

The general story is written for the layman who is referred to a glossary which explains the language which gradually grew around this new form of warfare. For those interested in the technical details of aeroplanes, their employment for fighting and the organization and training of the Corps, appendices are attached.

The book is freely illustrated with carefully chosen maps and photographs which make it easy to visualize the story.

It is a long cry from the wretchedly equipped half flight which opened the active service career of the Australian Flying Corps in Mesopotamia, to the four service squadrons, excellent both in personnel and machines that fought great air battles and gained much credit for Australia in the latter part of the war. It is notable that the first casualty in the ill-fated Mesopotamian half flight, which lost three out of its four officers, was a medical practitioner. This force labouring under extreme difficulties of material and climate set a fine standard of duty to the corps of which they were the pioneers.

The first complete squadron was formed in the Sinai desert and it too laboured for a long time under the handicap of poor machines, no match for their German opponents. This perhaps put its gallantry on a higher plane than in the concluding months of the war, when it gained such an ascendancy over the enemy that his aircraft would rarely accept battle, preferring the risk of landing in rough and wild country to an air duel with the deadly Bristol fighters and their Australian pilots. The history of this squadron is mainly one of long reconnaissance flights and bomb raids far into the enemy territory with ground attacks on small bodies of troops and air duels, in contrast to the massed air battles, bomb raids and ground attacks on large bodies of troops and railway centres of the Corps in France. One of the most remarkable feats of this squadron was the bombing of the Seventh Turkish Army in its retreat down the Wadi Fara, a narrow gully with precipitous walls, in the battle of Armageddon. For six hours an increasing bomb and machine-gun attack was carried out on the unfortunate Turks by No. 1. Australian and several British squadrons, causing immense casualties and entirely destroying this army as a fighting force.

The greater part of the volume is devoted to the fighting on the western front and it is easy to follow the clear account of the varying operations carried out by the three squadrons. Though the numerous air duels and battles make more dramatic reading, one is moved to admiration of the work done in artillery reconnaissances, carried out in machines not constructed for fighting and much inferior in flying qualities to the enemy scouts to whose attacks they were so exposed. The reader learns of the great moral and physical effect exercised by ground attacks on the enemy both in attack and retreat and considerable credit is claimed for the Air Force in the hold up of the German offensive in March, 1918. Mention is made of a formation of one hundred and five French aeroplanes which made an attack on the advancing enemy in this offensive. It is remarkable that in their bomb and machine gun attacks on troops on the ground pilots apparently were always able to distinguish our own from enemy troops and to locate new positions taken up in an advance so accurately.

The feelings of regret at the number of fine young soldiers who were killed in this Corps, are somewhat mitigated by the account of the far greater number of their opponents that they defeated.

The final chapter gives an account of the flights from England to Australia by Australian airmen.

The medical aspect of aviation is not considered.

Altogether the volume is one that should be read by all to whom thrilling adventure, gallantry and self-sacrifice by their fellow countrymen make an appeal.

<sup>1</sup> "The Official History of Australia in the War of 1914-1918: Volume VIII. The Australian Flying Corps in the Western and Eastern Theatres of War: 1914-1918, by F. M. Cutlack; 1923. Sydney: Angus and Robertson, Limited; Demy 8vo., pp. xxvii. + 485, with 55 illustrations, 19 maps and 10 sketch maps. Price: 18s. net.



## The Medical Journal of Australia

SATURDAY, FEBRUARY 9, 1924.

### The Transactions of Congress.

WITH our issue next week the first of a series of supplements containing the Transactions of the first session of the Australasian Medical Congress (British Medical Association) will appear. A delay of a few weeks has been unavoidable. The Executive Committee of Congress determined at a relatively early stage to make arrangements for the publication of the Transactions with much greater expedition than has been manifested in the past in connexion with previous medical congresses. Usually twelve months and at times even two years have elapsed between the holding of the meeting and the publication of the Transactions. The first British Medical Association Congress in the Commonwealth has been an unqualified success. That has been recognized by all. In a spirit of criticism, perhaps hypercriticism, we have ventured to express the opinion that the one defect was the excess of material. Eleven of the twelve Sections met twice a day from Tuesday to Friday and an enormous mass of papers formed the basis of the work of these bi-diurnal sessions. In addition the Section of Naval and Military Medicine and Surgery met on one occasion and lastly all the Sections went into combined session on the morning of Saturday, November 17, 1923. It is doubtful whether the Executive Committee realized or could have realized the total amount of contributions until the end of the Congress. In certain Sections the material assumed such alarming proportions that its publication resolved itself into a problem of ways and means as well as one of human achievement. The Executive Committee determined to have the Transactions published in a series of supplements to this journal, the first to appear early in January. A halt was called in order that the Committee could reconsider the probable cost. Various suggestions were made to overcome the difficulties that had

arisen from the fact that the total amount of material was nearly four times that anticipated and that the amount of tabular matter was so great that even if the additional cost could be met, it would have been almost impossible to find a printer able and willing to complete this technically difficult task in a satisfactory manner. The Executive Committee at first adopted the suggestion that authors of long papers should be required to shorten their contributions to approximately two thousand words each. But when it was discovered that this expedient was unacceptable to a certain number of authors, the Committee endeavoured to find a method that would give satisfaction without involving the Treasurer in an expenditure beyond the means at the disposal of the Committee. Each and every member of the Committee strained every nerve to find a solution of the problem. The President, Mr. G. A. Syme, and the Honorary General Secretary, Dr. A. L. Kenny, are well known as men who can always find some means to carry out what is desired and it is largely due to them that the several grave difficulties have been swept aside. Within three months of the end of the Congress the Transactions will appear in print. The Executive Committee, having given an undertaking, is honouring it. Large concessions have been granted to authors of papers of inordinate length, in view of the scientific importance of the contributions. Through the unstinted generosity of the Executive Committee and its willingness to proceed in the face of a certain amount of doubt concerning its full financial obligations, it has become possible to push forward with the work. The type is being set up by the Sydney and Melbourne Publishing Company, Limited, as the plant of the Australasian Medical Publishing Company, Limited, is not yet large enough to handle this extra work. There will be slight differences in type faces and some variations of the style of printing with which our readers have now become familiar. Every effort is being made to reduce these differences to a minimum and to present to the medical profession the Transactions in a readable and satisfactory form. Members are strongly recommended to preserve

their copies of the supplements as they appear. They will form when collected the record of Australia's most successful medical congress.

### Current Comment.

#### PAGET'S DISEASE OF THE NIPPLE.

PAGET's description in 1874 of the lesion of the nipple which bears his name, was mainly clinical. No histological observations were recorded and the commonly associated cancer in the breast substance was regarded as being secondary in nature. Since that time many observers have investigated the condition and diverse opinions as to the significance of its structure have been expressed. Some have held that the skin lesion is not itself malignant, but that it is of a pre-cancerous nature. Others have believed that it appears as a secondary manifestation to a primary scirrhus cancer of the underlying breast tissue. Again a parasitic theory of origin of the Paget cells has been invoked in order to explain the structure. Handley in 1919 stated that Paget's disease is essentially a primary carcinoma which starts in the smaller ducts of the breast. He thought that the change in the skin is nutritional and not malignant. He held that it is due to lymphatic obstruction caused by permeating masses of cancer cells. It will be remembered that in July, 1923, Dr. Keith Inglis made a preliminary communication in regard to his investigations into the nature of Paget's disease (see THE MEDICAL JOURNAL OF AUSTRALIA, September 1, 1923). He stated that Paget's disease is neoplastic *ab initio* and is to be regarded as a superficial cancer of low grade malignancy. He held that it always starts in the lactiferous ducts near the surface of the nipple. The second point on which he laid stress, was that the lesion extends from its site of origin by continuous spread both outwards on to the surface of the nipple and towards the areola and also downwards along the walls of the ducts to the acini. Scirrhus cancer is not the cause of the condition, but is the sequel. Dr. Inglis compared the relationship of Paget's disease of the nipple to scirrhus cancer with that of leucoplakia of the tongue to cancer of that organ.

An extremely interesting and important contribution to the subject has recently been made by Sir George Lenthal Cheatle.<sup>1</sup> In several important respects his conclusions coincide with those of Dr. Inglis. In the first place Sir George Lenthal Cheatle states that the disease always begins as a primary disease in epithelial cells situated above an imaginary line drawn parallel with the surface of the nipple immediately below the expansions that occur in the mammary ducts before they terminate upon the surface of that structure. A carcinoma beginning below this line is very rarely associated with Paget's disease of the nipple. Reference is made to two cases in which superficial carcinomata

began just below this imaginary line without inducing Paget's disease. At the same time Sir George Lenthal Cheatle refers at some length to one instance which, as he states, might at first sight appear as though Paget's disease was the secondary consequence to the upward spread of a subjacent carcinoma. In this instance the carcinoma was extensive and the superficial lesion of microscopical size. He states that it is hard to believe that so large a carcinoma could induce such a minute skin lesion. He suggests that in this instance either the skin lesion began independently or that it was the result of a cause similar to that which induced the appearance of the carcinoma. In endeavouring to prove that Paget's disease begins as a primary condition above the imaginary line referred to previously, he states that he cannot show a specimen in which the superficial lesion is not associated with a subjacent carcinoma. He states, however, that in all instances there is evidence of direct continuity between carcinoma in a duct and the lesion on the surface. He shows that this fact cannot be used as an argument in favour of the superficial lesion being secondary to the carcinoma, for if this were so, Paget's disease would be a very much more common condition than it is. Sir George Lenthal Cheatle refers to Sampson Handley's declaration that the disease is due to the plugging of the subjacent vessels by carcinoma cells. He describes two breasts affected by Paget's disease in which the carcinoma in the breast had not reached any lymphatic vessel and thus dismisses Handley's explanation.

In discussing his reasons for stating that the disease is essentially malignant Sir George Lenthal Cheatle describes in some detail specimens which are examples of the early stages affecting isolated areas. A few of the cells of the basal layers of epithelium have become separated from one another; they have become vacuolated; they have lost their prickles and among them may be seen cells undergoing mitosis. Connective tissue hyperplasia is regarded by him as being secondary in character. The masses of cells are never great enough to cause a fungating appearance on the diseased surface and with multiplication of the epithelial cells invasion of the deeper cells undoubtedly occurs. In the midst of the diseased areas can be seen epithelial cells including within them concentric bodies which compress the nuclei into semilunar shapes. The presence of these concentric cell inclusions is supposed by most observers to be typical of Paget's disease. Occasionally an epithelial cell nest can be seen. The disease generally begins in the pigment cell layer, but the resulting tumour is not pigmented.

In discussing the common association of carcinoma with Paget's disease, Sir George Lenthal Cheatle says that there must be a definite connexion between them. He draws attention, however, to two facts. The first is that the associated type of carcinoma varies with the types of epithelial cell that are affected; the second fact is that carcinoma in all parts of the breast is not always in direct continuity with the Paget's disease. He

<sup>1</sup> The British Journal of Surgery, October, 1923.

states that induction of carcinoma in the subjacent breast can occur in one of three ways. The first possibility is that the superficial tumour may grow downwards, using the mammary ducts as its pathway in the same way as lymphatic vessels act as viaducts for carcinomata. He refers to a specimen showing early involvement in carcinoma and points out that no normal epithelial lining is present in the early stages as would be the case if the duct were acting merely as a channel. The lining epithelium becomes the site of early primary disease. In the deeper parts of the carcinoma the structure may bear no resemblance to the carcinoma nearer the surface. Hence Sir George Lenthal Cheatle concludes that there must be something more than the mere downgrowth of a tumour. The second possibility is that portions of the disease upon the surface are detached and by means of transplantation become grafted and grow in the deeper parts of the breast. The third possibility is that the agents of irritation that produce Paget's disease of the nipple, may also be concerned in the production of the primary carcinoma in the epithelial cells of the breast and that induction occurs by way of the mammary ducts.

Many arguments are advanced against these possibilities and Sir George Lenthal Cheatle points out that in many breasts the carcinoma is seen mainly to affect one duct. He thinks that probably there are other reasons connected with the biology of the cells. The fact of one duct being affected more extensively than the remainder is capable of explanation if Dr. Inglis's conception of spread by direct continuity or contact is accepted. It is more difficult, however, to explain the occurrence of carcinomatous areas which have no apparent connexion with the superficial lesion. Sir George Lenthal Cheatle apparently accepts his third possibility that the agent of irritation which is producing Paget's disease, is also concerned in producing primary carcinoma in the epithelial cells of the underlying breast and that this is reached by means of the mammary ducts.

#### THE TRANSMISSION OF PLAGUE.

The flea *Xenopsylla cheopis* has been shown to be the common vector of plague to man. Its activities in this direction were the subject of discussion at the recent Pan-Pacific Science Congress. It was pointed out that the incidence of epidemics of plague was practically confined to areas corresponding to the distribution of *Xenopsylla cheopis*. Dr. E. W. Ferguson stated that this flea was the dominant variety all over the northern part of the continent of Australia and formed 47% of the rat flea population of Sydney. Professor C. J. Martin in the subsequent discussion elicited from Dr. Ferguson the fact that the latter had not been able to recognize *Xenopsylla astia* among the rat flea population, though it had frequently been the object of his search. Professor Martin referred to the fact that Madras though frequently the site of the introduction of plague had not been characterized by the occurrence of epidemics. *Xenopsylla astia* was the

prevailing flea in Madras and it was not a carrier. He thought that there was probably some biological reason for this.

This question has recently been investigated by Dr. J. Taylor and Dr. G. D. Chitre.<sup>1</sup> They endeavoured to determine whether or not *Xenopsylla astia* is capable of transmitting plague under certain climatic conditions. The experiments were carried out in Bombay. Madras City rats were used throughout. Out of eleven experiments with infected rats three successful transmissions were obtained with *Xenopsylla astia* and in a similar number under parallel conditions the number of successful transmissions with *Xenopsylla cheopis* was four. A series of transmission tests on the same lines was carried out with guinea pigs, eight being made with each variety of flea. Transmission was successful in six instances with *Xenopsylla cheopis* and in only one with *Xenopsylla astia*.

Drs. Taylor and Chitre conclude that under the conditions in Bombay at the time of experimentation *Xenopsylla astia* was capable of transmitting plague from rat to rat. They also state that the results suggest that *Xenopsylla cheopis* may be somewhat the better carrier of the two. On the small number of experiments made and with the close approximation of the results this conclusion cannot be justified. They recognize that the conditions of the experiment were not the same as those obtaining in every day life. Although transmission was obtained in Bombay with Madras City rats imported for the purpose through the agency of *Xenopsylla astia*, epizootic plague does not occur in Madras where these same rats and fleas abound. They offer two possible reasons for this apart from experimental conditions. There may be a difference in the climatic conditions and in the number of fleas per rat available. Under experimental conditions the number of fleas would be much higher than those naturally prevalent. They regard the climatic conditions as most important since it is evident that *Xenopsylla astia* can transmit plague in Bombay while it fails to do so in places such as Madras and Colombo.

Drs. Taylor and Chitre then tried to determine the habits of *Xenopsylla astia* in regard to biting man. They refer to the statement of Hirst that this variety of flea does not bite man in Colombo at temperatures above 26.5° C. (80° F.) and to Cragg's statement that in Agra it would feed on man, though not readily, at temperatures both above and below this level. A series of biting tests were carried out on the human host. Successful bites were obtained in 72% of instances within two minutes on a single application of each flea at temperatures varying between 25.5° C. and 28.8° C. The fleas in these experiments were applied to the forearm after having been removed from their rat hosts for about eighteen hours. Here again, though of interest, caution must be exercised in accepting these findings as indicative of the habits of the flea in question.

Drs. Taylor and Chitre recognize the necessity for further work on the bionomics of *Xenopsylla astia* under different climatic conditions.

<sup>1</sup> The Indian Journal of Medical Research, October, 1923.



## Abstracts from Current Medical Literature.

### PHYSIOLOGY.

#### The Chemical Regulation of Respiration.

R. GESELL (*American Journal of Physiology*, September, 1923) in a long paper reviews the various theories concerning the mechanism of the chemical control of the respiration, indicates where they fail and suggests a new point of view. In accordance with the theory proposed the activity of the respiratory centre is fundamentally a function of its own acidity as opposed to the acidity of the arterial blood, the specificity of carbon dioxide and the direct stimulating effect of lack of oxygen. By virtue of its sensitivity to the hydrogen ion the respiratory centre responds to changes in its own acidity as influenced by its own acid metabolism, the acid metabolism of the tissues as a whole and associated changes in the transport of acid. Evidence is presented indicating that carbon dioxide elicits acid effects by virtue of the properties of diffusion, carbon dioxide diffusing more rapidly than sodium bicarbonate. The intravenous injection of sodium bicarbonate not infrequently elicits hyperpnea in the presence of decreased hydrogen ion concentration of the arterial blood. Since such injection is not associated with an increased carbon dioxide content of the arterial blood, excluding the added sodium bicarbonate, the specific action of the  $\text{HCO}_3$  ion has been proposed. Another explanation is offered. Since the intravenous injection of sodium bicarbonate increases the freely diffusible  $\text{CO}_2$  and  $\text{H}_2\text{CO}_3$  molecules at the expense of the less freely diffusible dissociated H and  $\text{HCO}_3$  ions and furthermore since the rate of diffusion of the remaining dissociated acid is increased by the increase of the common  $\text{HCO}_3$  ion, it is suggested that in the presence of a semipermeable membrane a double mechanism exists producing diffusion of carbon dioxide against a positive gradient, whereas excessive elimination of carbon dioxide should elicit alkalemia, alkalosis and apnea, the intravenous injection of sodium bicarbonate might theoretically produce alkalemia, acidosis and hyperpnea. Experimental data support this view. The conception that the hydrogen ion concentration of the arterial blood regulates respiration is analysed and found wanting. Thus hyperpnea elicited by hemorrhage may be transformed into apnea by the intravenous injection of gum-saline solution. Apnea so elicited occurs as a result of an increased flow of unaltered blood through the respiratory centre. Since the injection of gum-saline solution increases the nutrient flow, such apnea occurs in the presence of increased flow of free

hydrogen ions to the respiratory centre. On the other hand the increased flow of carbon dioxide carriers improves the transport of acid from the centre. In the hyperpnea of anoxemia the blood is more alkaline than normal and the apnea elicited by abundant oxygen following such hyperpnea is associated with a sudden increased acidity of the arterial blood. It is suggested that the harmful effects respectively of hemorrhage and transfusion are probably due in the main to the accumulation of acid and lack of oxygen in the tissues consequent upon the altered transport of blood gases. Since hemoglobin is almost equally responsible for the transport of oxygen and carbon dioxide, the conclusion that hyperpnea of hemorrhage is an acid effect rather than a direct effect of lack of oxygen is open to question. Under normal conditions the amount of acid formed in the tissues is approximately equal to the amount of alkali liberated in the blood and consequently the diffusion of carbon dioxide from the tissues remains undisturbed. But when oxidations are being decreased while acids are being formed in unreduced amounts, the normal transport of acids from the centre is impaired, due to a reduced liberation of the potential alkalinity of the blood which passes through the centre. Since oxyhemoglobin cannot be reduced by the tissues so long as free oxygen is in solution in the plasma, it seems to follow that oxygen poisoning is due to the prevention of the liberation of the potential alkalinity of the blood. Unless the volume-flow of the blood is enormously accelerated, acidosis must obviously result. The production of lactic acid is also discussed at length. The conclusion is reached that lactic acid is an important regulator of respiration and that it exerts its effects under normal conditions as well as under conditions of stress by varying the numerator and denominator of the carbonate buffer system— $\text{H}_2\text{CO}_3$ —thereby govern-

ing the effectiveness of the free carbonic acid. In conclusion the following points are emphasized: Changes in acidity of the respiratory centre constitute the primary chemical control of respiration; changes in oxidation constitute a less direct control. But in so far as oxidation determines the kind and amount of acid formed and the efficiency of its transport and elimination, it is in the end the normal regulator of respiration.

#### Humoral Transmission of Nervous Excitation.

SOME years ago it was found by O. Loewi that if the liquid contained in a beating frog's heart after a strong stimulation of the vagus nerve, was transmitted to a second frog's heart, there appeared in this heart also the effects of vagus stimulation. R. Brinkman and E. Van Dam (*The Journal of Physiology*, August, 1923) have investi-

gated the question from a different point of view. The chemical processes following nerve stimulation may consist of ionic changes and of production of specific organic substances. As a suitable means of detecting small quantities of organic substances in the solution just leaving the surviving frog's heart the authors used the determination of the surface tension of this fluid. The general result of the experiments was that stimulation of the vago-sympathetic nerve with vagal effect was invariably followed by a decrease of the surface tension of the perfusing salt solution, but that stimulation with sympathetic action was always followed by a definite increase of this tension, so that it rose to the value of pure salt solution. The vagus influence was always accompanied by a decrease of surface tension of the perfusing saline solution, caused by the liberation of some slightly capillary active substance. A sympathetic action of the heart was also at once reflected in the saline solution by a sudden rise of the tension from a process by which the vagus substance was rendered inactive to the capillaries or prevented them dissolving in the fluid.

#### The Effects of Prolonged Sleeplessness in Man.

N. KLEITMAN (*American Journal of Physiology*, September, 1923) states that considering the importance of sleep for the human economy surprisingly few investigations have been made on the subject. He has attempted to gain some insight into the question by a study of experimental insomnia. Six young male adults underwent periods of experimental insomnia varying from forty to one hundred and fifteen hours. In order to prevent the subjects from sleeping it was found necessary that they should carry out almost continuous slight muscular exercise by moving about with short periods of rest. Careful observations were made. It was found that muscular relaxation induces sleep under normal conditions, but practically precipitates sleep under conditions of experimental insomnia. Blood sugar, alkaline reserve of the blood and plasma, percentage of hemoglobin, percentage of corpuscles, red and white cell count, body weight, basal metabolic rate, appetite, temperature, ability to name letters and to do mental arithmetic, all showed no variation from the normal during the period of sleeplessness. Respiration, heart rate and blood pressure showed a definite decrease in insomnia, but this decrease was mainly due to greater muscular relaxation of the sleepy subject. A Babinski reflex could be elicited in every subject tested during the sleep that followed insomnia. It is interpreted as indicating a functional block in the pyramidal system of fibres. There is a greater excretion of phosphates and acid at night; but on reversed routine with the subject sleeping in the day-



time this condition is reversed, indicating that increased secretion is due to sleep. The excretion of total nitrogen and of creatinin shows little diurnal variation and is unaffected by either insomnia or reversed routine. There is some evidence that the diurnal temperature variation is due to alternation of sleep and wakefulness and the temperature wave tends to be effaced during prolonged insomnia. The onset of sleep is probably due to complete muscular relaxation, voluntary or involuntary.

## BIOLOGICAL CHEMISTRY.

### Blood Changes in Polyneuritis.

T. J. THOMPSON and I. L. CARR (*Biochemical Journal*, April, 1923) have studied the variations in the amounts of different constituents of the blood of chickens during the development of polyneuritis. Polyneuritis was induced by feeding on a ration of boiled polished rice, filter paper and crushed marble. The chickens decreased in body weight and lost their appetites. They were laying at first, but gradually the number of eggs lessened and the chickens ceased to lay eggs. Sooner or later paralysis occurred. Blood was taken from the brachial artery under the wing. After some weeks the time of coagulation became so brief that it was not possible to obtain ten cubic centimetres of blood needed for the estimations. The authors determined the quantities of sugar, uric acid, creatinin and total non-protein nitrogen in the blood. They found considerable variations in the amounts of these constituents in the chickens before the experiment. No constant or considerable changes were noted in the percentages of sugar or non-protein nitrogen as the experiment progressed. The percentage of uric acid and of creatinin increased in the blood shortly before the onset of polyneuritis. Autopsies of those chickens which died, revealed deterioration in the heart, kidneys and liver. The authors conclude that disintegration of these organs accounts for the increased amounts of uric acid and creatinin in the blood. When the paralysis was so advanced that the chickens could not walk, they were given thirty grammes of yeast daily. Three out of eight chickens recovered.

### Nutrition of Pigeons.

K. SUGIURA and S. R. BENEDICT (*Journal of Biological Chemistry*, January, 1923) have made a study of the nutrition of the pigeon. Although pigeons have been frequently used in investigations of anti-neuritic vitamin, no previous work has been done on their nutrition generally. The authors have been concerned with the adequacy of a synthetic diet for the growth, maintenance and reproduction of pigeons and with the question of the significance of the fat soluble vitamin in the nutrition of pigeons.

The basic ration has consisted of casein twenty-two, cane sugar ten, starch twenty-seven, agar two, salt mixture three, butter fat thirty and yeast six. It has been shown to be adequate for white rats. The pigeons have been of mixed origin and have had a normal diet of corn, Kaffir corn, wheat, buckwheat, rice, barley and hemp seeds. Experiments of feeding with five, ten, fifteen and twenty grammes daily of the basic ration with controls of normal diet, showed that fifteen grammes of synthetic diet sufficed to maintain weight. On this fifteen gramme ration egg production has been normal. The size of the eggs has not diminished, but the yolk has a different yellow colour. Female pigeons have been mated with male pigeons to ascertain whether the eggs have been fertile. The young have been fed on the synthetic diet. The young pigeons show no weakness in legs or wings and no abnormality except in the colour of the skin of the legs. Butter has been replaced by lard in the basic diet and fat omitted altogether, being replaced in part by cane sugar. Pigeons grow well and maintain weight on these diets. Provided the daily number of calories is sufficient, they lay eggs. It would thus appear that fat soluble vitamin is not essential in any stage of avian nutrition. It is further obvious that pigeons require no anti-scorbutic vitamin.

### Purification of "Insulin."

H. W. DUDLEY (*Biochemical Journal*, April, 1923) has tried to purify "Insulin" and to determine its general chemical characters. The "Insulin" has been prepared from fresh ox pancreas by treating with 95% alcohol for several hours and by evaporating the filtrate to small bulk. After removal of the fats excess of absolute alcohol precipitates a white solid which contains the active principle. This "crude 'Insulin'" is a white hygroscopic powder very soluble in water in which it dissolves to form a slightly acid straw-coloured fluid. The yield varied in different samples, but averaged 0.7 gramme per kilogram from one hundred and three kilograms of ox pancreas. About five milligrammes of crude "Insulin" corresponding to fifteen grammes of pancreas is needed to cause hypoglycæmic convulsions in a rabbit weighing two kilograms. Crude "Insulin" consists of 50% mineral matter and yields biuret, Millon, glyoxylic acid, iminazole, Molish carbohydrate and Seliwanoff fructose reactions. By treatment of a solution of "crude 'Insulin'" with picric acid and insoluble picrate is formed. A rabbit unit of picrate is one milligramme. This picrate can be converted into a soluble hydrochloride. The hydrochloride contains no organically combined phosphorus. The tryptophane and Millon reactions are absent. Organic sulphur is present. Iminazole reaction is intense. Both pepsin and trypsin destroy "Insulin." From solu-

tions of the hydrochloride precipitates may be formed by the careful addition of alkali and of acid. Both precipitates are more potent than the original hydrochloride in causing hypoglycæmic convulsions in rabbits. "Insulin" can be filtered through a Berkefeld filter if its reaction is made slightly alkaline to the "iso-electric point."

### Estimation of Ammonia and Urea.

S. LEVY-SIMPSON and D. C. CARROLL (*Biochemical Journal*, March, 1923) hold that they have devised a rapid yet accurate method for the estimation of ammonia and urea in urine and in other fluids. The method depends on the steam-distillation of ammonia from alcoholic solutions. About five cubic centimetres of fluid containing ammonia is mixed with ninety cubic centimetres of alcohol and the mixture is distilled with steam into standard acid solution. Frothing of the fluid indicates that the alcohol has been driven over. The authors show that 90% of alcohol increases the rate of distillation so that all ammonia has passed over before frothing commences. By use of a time analysis curve the authors hold that it is possible to determine whether correct results are being obtained when working with unknown quantities of ammonia. By treating urea solutions with urease this method can be used to estimate urea. A complete determination of urea and of ammonia can be made in urine with one apparatus in thirty minutes, including the time for the conversion of urea into ammonium carbonate. A determination of ammonia only requires seven minutes. The authors consider that the accuracy, rapidity and facility of manipulation which the method possesses, render it more desirable as a means of estimating ammonia and urea than any of the methods at present in use.

### Concentration of "Insulin."

P. J. MOLONEY and D. M. FINDLAY (*The Journal of Biological Chemistry*, September, 1923) describe a method for concentrating "Insulin" by adsorption on benzoic acid. In the preparation of "Insulin" on the large scale, the concentration of dilute aqueous solutions of potent material offers difficulties. The potent material can be adsorbed by charcoal, but it is not easy to recover the active principle from the carbon. The authors have tried the use of a reagent which could be used in a finely divided form and which could be subsequently dissolved. The authors have tested benzoic acid which can be dissolved as a salt and precipitated as benzoic acid after acidification. The method of precipitating "Insulin" with benzoic acid is successful with solutions containing five units in each cubic centimetre. The method has been used to concentrate the original alcoholic extract of the gland on the large scale.

## Medical Societies.

### THE SYDNEY HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE SYDNEY HOSPITAL CLINICAL SOCIETY was held in the lecture hall at the Sydney Hospital on August 30, 1923, Dr. T. FIASCHI, D.S.O., the PRESIDENT, in the chair.

#### Sclerosis of the Brain Stem.

DR. H. HAMILTON MARSHALL showed a labourer, *atatis* fifty-four years, who complained of shakiness of the right hand of seven months' duration. The patient had suffered eighteen months before from a condition of the left hand analogous to Raynaud's disease and had recovered. On examination a definite tremor of the right hand was evident and this was increased considerably when he tried to perform any voluntary movement. There was complete anaesthesia of the left side of the body except for a small area over the malar bone. There was no swelling of the optic disc, no headache or other evidence of cerebral tumour. There had been no response to the Wassermann test applied to blood and cerebro-spinal fluid. The condition had developed slowly and was apparently progressive. Dr. Marshall had consulted Professor J. I. Hunter at the University and they had concluded that a lesion on the right side of the *crus cerebri* affecting the fillet and fibres from the red nucleus would explain the symptoms. The centre for the fifth nerve which gave origin to the fibres supplying the skin over the malar bone was the highest part of the fifth nerve nucleus and had escaped damage. This small area of anaesthesia helped in the localization of the level of the lesion. The remaining fibres of the fifth nerve were affected in this patient. Dr. Marshall thought the condition was due to a sclerosis of the brain stem and that possibly arterial spasm had been a primary factor in inducing the sclerosis. The lesion was a most unusual one and was quite unlike that of any well recognized entity. The opinion was expressed by several members that Dr. Marshall's diagnosis was the most probable one.

#### Lymphangioma of the Hand.

DR. GEORGE BELL, O.B.E., showed a girl aged twenty-three years, who complained of swelling of the index finger of the left hand since birth; the swelling had increased in size recently. The patient had suffered with macrodactylism of the middle finger of the left hand; this finger had been amputated some years previously. The swelling of the index finger caused disability and pain.

Examination revealed a much enlarged wedge-shaped finger with swelling of the outer aspect of the finger and palm, suggesting a varicosity of the lymph spaces. The swelling was soft and doughy. It was agreed that lymphangioma was the most probable diagnosis and amputation of the finger was recommended since it would be inexpedient to endeavour to dissect out the lymph channels.

DR. KEITH INGLIS showed a fetus, at nearly full term, in which there was definite enlargement of two fingers of the left hand, similar to the enlargement in Dr. Bell's patient. The enlargement in this fetus was due to lymphangioma and there were other lymphangiomatous tumours over the thorax and abdomen.

#### Lympho-sarcoma.

Dr. Keith Inglis also showed the stomach, kidneys and a mediastinal growth from patients who had suffered from lympho-sarcoma. He pointed out that there was a tendency for the shape of the organ affected to be retained, even when everywhere invaded by lympho-sarcomatous tissue. In one instance the tumour had grown round the affected organ without altering its shape. The kidney was enlarged and there were masses of leucocytes to be seen between the tubules and cells much as in leucæmia. The stomach was enlarged, very thick walled (about 7.5 centimetres thick on the greater curvature) and extremely pale in colour. The texture was firm and the organ weighed five kilograms (eleven pounds). It was pointed out that all gradations occurred between leucæmia and

lympho-sarcoma and that in some cases differentiation was difficult. It appeared that there was a disturbance or tumour-like growth of the bone marrow in some instances.

#### Tuberculosis of the Testis.

DR. GEORGE BELL showed two adult males suffering from tuberculous disease of the testis. A firm somewhat nodular swelling involved the epididymis in each instance. In neither of these patients was there evidence of tuberculous disease elsewhere. Dr. Bell showed the patients for the purpose of discussing the treatment. It was agreed that the systematic injection of tuberculin, accompanied by other treatment appropriate to tuberculosis, held out the best prospects for recovery.

#### Tuberculous Ulceration of the Pharynx.

DR. A. HOLMES A COURT brought forward a man, aged thirty-four years, who had been suffering from chronic ulceration of the posterior pharyngeal wall for six months. The condition had originally been regarded as probably due to syphilis, but the blood had not given a Wassermann reaction and microscopical examination of a stained section from a snipping of a tumour had disclosed a simple granuloma. Further examination had revealed signs in the middle lobe of the right lung. Following a diagnostic injection of old tuberculin a definite general and focal reaction had occurred and after numerous examinations the tubercle bacillus had been found in the sputum. Remarkable improvement had followed tuberculin treatment and the ulcer which had been larger than a shilling, had become only about the size of a pea.

#### Hysteria.

Dr. Holmes A Court's second patient was a woman of thirty-two years, who had been bed-ridden for ten years. She was said originally to have suffered from pulmonary tuberculosis and had been advised to remain in bed. This she had done, the tuberculous focus had rapidly healed, but the patient had remained in bed because she had been advised to do so. Physical examination at the end of ten years had revealed no active tuberculosis. The anterior tibial muscles of the left leg were in a condition of atrophy from disuse resulting from foot drop, the left knee was fixed by fibrous ankylosis and there was a minor grade of arthritis of the right hip joint. As a result of treatment the patient was able to walk and there appeared to be a good prospect of complete restoration of function.

#### Skilagrams.

Drs. J. G. AND W. A. EDWARDS demonstrated a number of X-ray pictures of unusual interest. These included skilagrams, of tuberculosis of carpal bone (*os lunatum*), Colles' fracture with unusual displacement, extensive spondylitis in the lumbar region, a retro-caecal appendix filled with barium sulphate, an unusually long appendix, pituitary tumour with definite erosion of the anterior clinoid processes and a gun shot wound of the ilium showing a round, clear cut hole as if made by a trephine.

#### Arthritis Deformans.

DR. LESLIE DUNLOP showed a middle-aged man suffering from advanced *arthritis deformans*. The changes in the joints were mainly peri-articular. He had suffered considerable pain and movement of many joints had been very limited before treatment.

Intravenous injections of *Bacillus coli* vaccine had been given, beginning with fifty million organisms and increasing up to eight hundred millions. The pain had been much relieved and movement had increased, especially in the right knee joint where the range of movement was ninety degrees. Formerly it had been only ten degrees in this joint. Ulnar deflection was unaltered.

#### Umbilical Sinus.

DR. H. S. STACY showed a boy, aged five years, who had suffered from a discharging sinus in the neighbourhood of the navel since birth. The sinus had been dissected out. There had been no communication with the peritoneal cavity, but the sinus had reopened and was again discharging. The application of the actual cautery was recommended.

**Traumatic Neurasthenia.**

Dr. Stacy's second patient was a young man who had sustained an injury to the upper dorsal region of his vertebral column. X-ray examination demonstrated a minor degree of scoliosis in that region. The patient complained of diffuse pain in the region of the injury, to account for which no anatomical lesion could be discovered. During the discussion which ensued, it was suggested that the condition might be regarded as a traumatic neurosis.

**Paralysis of the Median Nerve.**

DR. REGINALD BRIDGE showed two patients. The first had received an incised wound on the inner aspect of the right arm and was recovering from the effects of a palsy of the right median nerve. The ends of the nerve had been found after some difficulty and united. The result was satisfactory.

The second patient had sustained a fracture through the upper third of the shaft of the left humerus and this injury had been followed at a considerable interval of time by paralysis of the left median nerve. The functional result had been poor. A surgeon had performed an operation to improve function and the paralysis had followed the operation. It was a question whether the paralysis was due to callus formation or pressure on the nerve. There were signs of recovery of function and passive and active movements of the shoulder joint were all the treatment necessary at the moment.

**THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.**

A MEETING OF THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA was held at the University of Adelaide on August 3, 1923.

**Aspiration of a Tonsil into the Lung.**

DR. R. H. PULLEINE read a letter from Dr. Chevalier Jackson, of Philadelphia, in regard to a case of aspiration of a tonsil into the lung, which Dr. A. A. Lendon had reported at a previous meeting. The history of this patient was published in the issue of the journal of November 10, 1923, page 494.

**Foreign Body in the Bronchus.**

DR. C. T. TURNER reported the history of a child, aged two years, who had been brought to the Adelaide Hospital two years previously suffering from the presence of a foreign body in the air passages. Tracheotomy had been performed, but the foreign body had been situated below the level of the site of operation and the child had died very shortly afterwards. At *post mortem* examination it had been found that one bronchus was completely shut off by half an ordinary green pea. The other lung had been completely atelectatic. The obstruction had thus blocked the only lung which was functioning.

**Fireman's Cramp.**

DR. R. L. T. GRANT referred to a case of fireman's cramp, which he had reported on July 7, 1922. He said that Professor Cleland had drawn his attention to the review of a paper by K. M. Moss in a recent issue of *The British Medical Journal*. Dr. Moss had offered an explanation of the origin of this condition. He had stated that miners and others who worked hard in an over-heated atmosphere, suffered very greatly from thirst which was in part due to the drying of the mouth and throat. The amount of water drunk by inexperienced men under these conditions was greatly in excess of the needs of the body, while the loss of sodium chloride by sweating was not so compensated. The result of this was to bring about water poisoning of the muscles and consequent cramp.

PROFESSOR C. J. MARTIN, F.R.S., said that he was acquainted with the details of the investigation to which Dr. Grant had referred. As showing the extent to which sweating under these conditions might lead to loss of water and sodium chloride from the body, Professor

Martin pointed out that one of the best miners working in a heated atmosphere could lose as much as eight kilograms (eighteen pounds) of water in a five-hour shift. If he were careful he drank only three to three and a half litres of water. These men had a capacity for sweating which was not attained by the average individual. Since this sweat would contain from 0.2% to 0.3% sodium chloride, such an output of sweat would involve a loss of from fifteen to twenty grammes of chloride in five hours. This was more than the normal output for twenty-four hours. Under these conditions the urine became chloride free and if water were consumed in quantity, dilution of the tissues must result. Such dilution with its consequences might be obviated by drinking an 0.2% solution of sodium chloride instead of water. The chlorides in sweating were not derived directly from the blood, but were a product of selective secretion, since 40% of the total chloride consisted of chloride of potash.

PROFESSOR J. B. CLELAND pointed out that it had frequently been suggested that chronic interstitial nephritis was more frequent in Australia than in Europe and that the hot, dry climate resulting in a greater output of fluid from the skin with concentration of the urine caused a greater strain to be thrown upon the renal apparatus. He asked Professor Martin whether miners were specially liable to kidney disturbances of this nature.

PROFESSOR MARTIN said that he was unaware of any evidence which would justify this conclusion.

DR. A. A. LENDON stated his impression that there was less kidney disease in Australia than in England.

DR. W. RAY pointed out that the excessive loss of water in individuals such as those cited by Professor Martin would of necessity place a great strain upon the circulation, if the fluid were ultimately derived from the blood. He inquired whether any estimation of blood volume had been made in the course of these experiments.

PROFESSOR MARTIN said that as far as he knew no such observations had been made.

**Dilatation of the Stomach.**

DR. R. H. PULLEINE referred to the common belief that oatmeal water was less dangerous than pure water and cited a case which had come under his notice at Gympie, in Queensland. He had been called at about six o'clock in the evening to see a miner who, after working at a considerable depth, had gone home suffering intense abdominal pain. He had sent for "a shilling's worth" of rum; on swallowing this his distress and collapse had become more severe. It had been obvious that the man was suffering from extreme dilatation of the stomach. Dr. Pulleine had left the house to procure a stomach tube. Before he had been able to return the man had died. At *post mortem* examination he had found an enormously dilated stomach which was nearly full of oatmeal.

**Proteolytic Enzymes and Azine Dyes.**

MR. R. H. MARSTON gave an account of researches upon which he had been engaged for a period of three years on the compounds formed by the proteolytic enzymes with the various azine dyes. His experiments indicated that the most highly purified proteolytic enzymes procurable consisted of something over 98% of inert material and that with the aid of azine dye such as safranin a fraction not exceeding 2% of the weight of the most highly purified trypsin or pepsin might be precipitated. From this very small amount of precipitation 70% of the original activities could be recovered and the fluid from which the precipitate had been removed, would be proteolytically inactive. No other enzymes so far investigated with the exception of the proteolytic enzymes were precipitated by these dyes. On the other hand all the proteolytic enzymes, pepsin, trypsin, erepsin and the vegetable proteolytic enzymes were precipitable by enzymes. These facts suggested that the enzyme attached itself to the protein molecule by an azine structure present in the protein. If proteins were built up out of amino acids which united at their extremities, as was customarily supposed, there would be no azine structures in the protein molecules. If, however, the amino acids constituting the protein molecule



were linked together in pairs, each pair constituting a diketopiperazine ring, then each pair of amino acids in the protein molecule would present an azine structure and a point of union for the enzyme. The existence of anhydrides of amino acids in solutions resulting from the hydrolysis of proteins had frequently been quoted by other observers.

PROFESSOR BRAILSFORD ROBERTSON drew attention to the analogy between this theory of the structure of the protein molecule and the structure of urea as recently established by E. A. Warner. He also pointed out that this conception of the structure of the protein molecule enabled observers to understand why the only free amino groups in a protein molecule were those which corresponded to half the amino nitrogen in the lysine which the protein molecule contained. A catenary structure of the protein molecule would inevitably involve the existence of at least one free amino group at the extremity of the molecule and the existence of such a protein as zein which contained no free amino groups at all, would be incomprehensible.

#### Carbo-hydrates and Starvation.

DR. A. R. SOUTHWOOD reported a series of observations upon himself and others concerning the effect of a period of carbo-hydrate starvation upon the capacity for storing or otherwise utilizing carbo-hydrates. He had found that after a period of thirty-six hours carbo-hydrate starvation the ingestion of fifty grammes of glucose was followed by considerably greater change of blood sugar concentration and a more prolonged rise of blood sugar than that observed under normal conditions. The simultaneous administration of "Insulin" prevented this extreme rise of blood sugar and abbreviated the period of glucœmia to that which was normally observed. The appearances suggested that a period of carbo-hydrate starvation rendered the pancreas temporarily and comparatively inactive.

#### Hookworm.

PROFESSOR HARVEY JOHNSTON exhibited two stages in the life-cycle of the infective larvæ of hookworm. These larvæ had been taken from soil saturated with fæces in Queensland and had undergone their first moult. It was after the first moult that they were able to enter the skin. One of the larvæ had succeeded in gaining entry into a guinea pig's skin and a section of the skin showed the larvæ embodied in it.

#### Trematodes.

Professor Harvey Johnston also exhibited trematodes obtained from the coeca of water hens in the Adelaide Botanical Gardens. These trematodes belonged to two genera which had not previously been described as occurring in that part of the world. One of them belonged to a genus which occurred in the same type of host in Central Europe. The parasite had undoubtedly undergone evolution along with its host.

## British Medical Association News.

### NOMINATIONS AND ELECTIONS.

THE following have been nominated for election as members of the New South Wales Branch of the British Medical Association:

DARRAGH, WILLIAM CHANDLER, M.B., Ch.M., 1923 (Univ. Sydney), Lucy Street, Ashfield.

HUGHES, THOMAS DIXON, M.B., Ch.M., 1922 (Univ. Sydney), Women's Hospital, Crown Street, Sydney.

TAYLOR, CHARLES MALCOLM, M.B., Mast. Surg., 1921 (Univ. Sydney), Dumbarton, Ashton Street, Waverley.

THOMPSON, JOSEPH GEORGE, M.B., Ch.M., 1923 (Univ. Sydney), 10, Macarthur Parade, Dulwich Hill.

WATSON, ALBERT LESLIE, M.B., Ch.M., 1923 (Univ. Sydney), Marrickville Hospital, Marrickville.

THE undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

ASHBY, HARRY LAWTON, M.B., Ch.M., 1923 (Univ. Sydney), Barellan.

ASHER, MAISIE HEATH, M.B., Ch.M., 1923 (Univ. Sydney), 30, Eglinton Road, Glebe Point.

EWAN, GREY LAMONT, M.B., Ch.M., 1922 (Univ. Sydney), Mental Hospital, Gladesville.

TAYLOR, HENRY JOHN, M.B., Ch.M., 1923 (Univ. Sydney), Townsville Hospital, Townsville.

WILLIAMS, DARCY AMBROSE, M.B., Ch.M., 1923 (Univ. Sydney), 73, Boulevard, Dulwich Hill.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

BREW, GEORGE ALEXANDER, M.B., B.S., 1923 (Univ. Melbourne), 139, Stevenson Street, Kew.

COMMONS, PHILIP GRAHAM, M.B., B.S., 1923 (Univ. Melbourne), Hawthorn.

## Post-Graduate Work.

### POST-GRADUATE COURSE IN ADELAIDE.

THE Post-Graduate Courses Committee of the University of Adelaide announces that the course in medicine planned to be held in March, 1924, has been postponed. The Committee proposes to hold a course in October, 1924, provided that the number of practitioners notifying their intention to attend warrants it.

A course of instruction on the administration of "Insulin" in diabetes will be held on March 14, 1924. This course will consist of a lecture at half past nine o'clock in the Darling Building by Professor T. Brailsford Robertson on the chemistry and physiology of diabetes; a demonstration at half past ten o'clock of the pharmacological action of "Insulin" and of the methods of estimating the sugar content of the blood and urine by Professor T. Brailsford Robertson, also in the Darling Building; a demonstration at two o'clock at the Children's Hospital of patients under treatment with "Insulin," by Dr. C. T. C. de Crespigny; and demonstrations at the Adelaide Hospital from half past three till half past five o'clock of patients treated with "Insulin" by Dr. W. Ray and Dr. F. S. Hone.

The fee for this course is ten shillings and sixpence. Practitioners desirous of attending should notify the Registrar of the University before March 1, 1924, and at the same time forward the amount of the fee.

## Correspondence.

### CARDIAC ARRHYTHMIA.

SIR: I have read your review of "Cardiac Arrhythmia and the Neo-cardiology" and I shall content myself for the present with showing you what your reviewer has done.

He attempts a quotation thus: "This tracing illustrates the occurrence of one so-called premature beat immediately following the diastolic wave after the first powerful beat. No other such diastolic line is seen in the rest of the tracing. The pulse rate in this case was thirty-three per minute, which we understand from the neo-cardiologists to constitute the condition known as that of heart block (*sic*). Clearly, therefore, premature beat co-exists or alternates with the condition known as heart-block."



This is what I wrote: "This tracing illustrates the occurrence of one so-called Premature Beat immediately following the Dicrotic Wave after the first powerful beat. No other such break in the diastolic is seen in the rest of the tracing. The pulse rate in this case was 33 per minute, which we understand from the Neocardiologists to constitute the condition known as that of Heart Block. Clearly, therefore, the Premature Beat co-exists, or alternates, with the condition known as Heart Block."

More than ten mistakes, material or clerical, in the so-called quotation of a passage of four and a half lines in length.

Your reviewer seems to have as little capacity for accurate quotation as he has sound knowledge of the subject of arrhythmia.

His amateurish scramble is an expression of slovenly puerile ineptitude.

If you throw pebbles at my back windows you must not be surprised if I retaliate upon your conservatory.

And that, like rosemary, is for remembrance.

Yours, etc.,

ALFRED WEBSTER.

229, St. George's Terrace, Perth,  
January 16, 1924.

[Dr. Webster has cause for complaint. The sentence including the words "break in the diastolic" was wrongly copied from the manuscript of the review before being set and the error escaped our notice. Our reviewer who was selected because he is one of the most eminent authorities on diseases of the heart in Australia, is not responsible for this error. The substitution of small for capital letters in words which are not proper nouns, and the elision of commas in certain positions have been deliberate and should not be regarded as errors.—EDITOR.]

## HERPES AND VARICELLA.

SIR: In the last issue of THE MEDICAL JOURNAL OF AUSTRALIA (January 19, 1924) a letter appears upon the above subject by Dr. A. E. Vivian.

Much correspondence has been taking place of recent years upon this subject in *The British Medical Journal* and other journals. Many writers describe cases of coincidental attack of *herpes zoster* and varicella. Other writers question that there is any relationship between these two diseases. In connexion with this matter I desire to record some experience I had in regard to two patients I saw in consultation at the Caulfield Military Hospital in 1918. These patients, returned soldiers, had typical *herpes zoster* with an accompanying generalized herpetic eruption.

Case I.—*Herpes zoster* (right thoracic) with generalized herpetic eruption: This eruption came out in more or less crop-like fashion, during the second to fifth days, after the first appearance of the *herpes zoster*. The vesicular lesions upon the scalp were so numerous as to suggest a double *zoster* of the head. The lesions upon the legs, trunk and arms were more scattered, as seen in varicella.

Case II.—*Herpes cervico-brachialis*, right side, with generalized herpetic eruption coming out during the first four days after first appearance of the *zoster*: The accompanying herpetic eruption affected the head, arms, trunk and legs. Lesions were not so numerous as in the previous case.

After a very careful examination I formed the opinion that the accompanying generalized herpetic eruptions in these patients were not varicella. I took the opportunity of getting the opinion of Dr. Johnson, of the Board of Health, who has had a very large experience in varicella, especially in adults. After a careful examination of these patients, he formed the same opinion as myself, that they were not cases of *herpes zoster* with varicella occurring simultaneously, but really *herpes zoster* with generalized herpes eruption.

Darier states that he has only on one occasion seen *herpes zoster* with a generalized herpes eruption and that

the case came under his notice during a small-pox scare. Curiously enough it was during a small-pox scare that these patients came under my notice. Dr. Johnston and myself in conversation came to the conclusion that these two cases were the only ones of which we had had personal knowledge and that we had never seen varicella and *zoster* occurring at the same time.

Yours, etc.,

HERMAN LAWRENCE.

Lister House,  
63, Collins Street, Melbourne,  
January 22, 1924.

## FEDERAL INCOME TAX DEDUCTIONS.

A CORRESPONDENT writes that he bought a second-hand Ford car in July, 1921, for the sum of £200. In February 1923, he sold this car for £100 and bought a new Hupmobile car for £590. He wishes to know what deductions he can claim in his return for Federal income tax purposes.

IN THE MEDICAL JOURNAL OF AUSTRALIA of July 22, 1922, we published an article by Messrs. H. L. Cunningham and Robert J. Stiffe on Federal income tax. In this article will be found much information to enable readers to make their returns. We are prepared to republish this article in pamphlet form if there is a demand for copies.

A deduction of 10% for depreciation is allowed on motor cars. The Federal Income Tax Commissioners do not allow any deduction for replacement of motor cars, although replacement is allowed in respect of instruments used in practice. For the year ended June 30, 1922, no deduction is allowable, because it is specifically stated that there is no recognized depreciation on motor cars purchased during the period covered by the return. For the year ended June 30, 1923, the sum of £11 13s. 4d. may be deducted in respect of the Ford car up to the date of sale (seven months). By selling the car for £100 our correspondent has to bear the cost of the remaining £83 6s. 8d.. Similarly no deduction for depreciation is allowed in respect of the Hupmobile car during the year ended June 30, 1923. During the year ended June 30, 1924, the sum of £59 can be deducted. Any sums actually spent on repairs can be deducted in the return.—EDITOR.

## Analytical Department.

### "PEPSODENT TOOTH PASTE."

IN our issue of August 25, 1923, page 204, we published a report on "Pepsodent Tooth Paste." In this report the results of analyses were set out, the amount of hydrochloric acid being given as from 0.158% to 0.164%. The question has been raised whether this should be taken to imply that the contained hydrochloric acid is free in the paste or whether it is the amount of titratable acid. The figures given represent the titratable acidity expressed as hydrochloric acid. The true acidity is much less. The greater part of the hydrochloric acid added in the process of manufacture is neutralized by the calcium phosphate,  $\text{CaHPO}_4$ ,  $\text{Ca}(\text{H}_2\text{PO}_4)_2$ , and calcium chloride being formed. Expressing the acidity in terms of the hydrogen ion concentration "Pepsodent Tooth Paste" has a pH of 4.7 — 5, that is, it is distinctly acid. This is about the lowest acidity at which pepsin produces any action whatsoever on proteins and the action is but slight. This still further confirms our opinion that the pepsin of "Pepsodent Tooth Paste" can have little effect on the protein film covering the teeth.

The first samples of "Pepsodent Tooth Paste" examined, which were recently prepared, attacked gelatine very slightly but still appreciably; a sample recently purchased and examined had no appreciable effect on gelatine.

## Proceedings of the Australian Medical Boards.

### TASMANIA.

THE undermentioned have been registered, under the provisions of *The Medical Act, 1918*, as duly qualified medical practitioners:

CLARKE, RALEIGH, M.B., B.S., 1923 (Univ. Melbourne), St. Helens.

EDGERTON, ELLEN CURTIS, M.B., B.S., 1919 (Univ. Melbourne), St. Helens.

STEELE, WILLIAM HUEY GERARD, M.B., B.S., 1923 (Univ. Melbourne), Queenstown.

## Medical Appointments.

DR. A. A. LENDON (B.M.A.) has been appointed President of the Medical Board of South Australia.

THE undermentioned have been authorized by the Board of Health of New South Wales as inspectors under the *Cattle Slaughtering and Diseased Animals and Meat Act, 1902*: DR. J. R. ALLISON (B.M.A.), at Coraki; DR. A. R. SCOTT-ORR (B.M.A.), at Milton.

DR. E. A. JOHNSON (B.M.A.) has been appointed temporarily as Deputy Inspector General of Hospitals in South Australia.

THE undermentioned have been appointed Resident Medical Officers at the Adelaide Hospital: DR. W. R. ANGUS, DR. J. R. CORNISH, DR. D. A. DOWLING, DR. G. H. HOWARD, DR. A. J. LEWIS, DR. A. L. TOSTEVIN, DR. L. D. COWLING, DR. H. C. HOSKING, DR. J. S. KESSELL, DR. F. L. THYER, DR. F. R. WICKS.

DR. T. L. BARKER has been appointed District Medical Officer and Public Vaccinator at Corrigin, Western Australia.

DR. S. K. CROWNSON has been appointed Resident Medical Officer at the Government Hospital, Kalgoorlie, Western Australia.

DR. A. R. BEAN (B.M.A.) and DR. H. I. CARLILE (B.M.A.) have been appointed Justices of the Peace for the York and Mount Margaret Magisterial Districts, respectively, in Western Australia.

THE following appointments have been made at the Fremantle Public Hospital, Western Australia: DR. RICHARD GREEN (B.M.A.) as Senior Resident Medical Officer; DR. M. D. H. HARPUR (B.M.A.) as Junior Resident Medical Officer.

THE undermentioned have been appointed Junior Resident Medical Officers at the Perth Hospital: DR. G. R. DAVIDSON, DR. M. A. MAYRHOFER, DR. H. J. R. THORNE.

DR. SARAH V. MCCONNEL has been appointed Resident Pathologist at the Perth Hospital.

DR. J. J. KELLY (B.M.A.) has been appointed Public Vaccinator at Wangaratta, Victoria.

## Medical Appointments Vacant, etc..

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xviii.

MENTAL HOSPITAL, PARKSIDE, SOUTH AUSTRALIA: Junior Medical Officer.  
SYDNEY HOSPITAL: Part-time Bacteriologist.

## Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney	Australian Natives' Association Ashfield and District Friendly Societies' Dispensary Balmain United Friendly Society's Dispensary Friendly Society Lodges at Casino Leichhardt and Petersham Dispensary Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney Marrickville United Friendly Societies' Dispensary North Sydney United Friendly Societies People's Prudential Benefit Society Phoenix Mutual Provident Society
VICTORIA: Honorary Secretary, Medical Society Hall, East Melbourne	All Institutes or Medical Dispensaries Australian Prudential Association Proprietary, Limited Mutual National Provident Club National Provident Association
QUEENSLAND: Honorary Secretary, B. M. A. Building, Adelaide Street, Brisbane	Brisbane United Friendly Society Institute Stannary Hills Hospital
SOUTH AUSTRALIA: Honorary Secretary, 12, North Terrace, Adelaide	Contract Practice Appointments at Renmark Contract Practice Appointments in South Australia
WESTERN AUSTRALIA: Honorary Secretary, Saint George's Terrace, Perth	All Contract Practice Appointments in Western Australia
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington	Friendly Society Lodges, Wellington, New Zealand

## Diary for the Month.

- FEB. 12.—New South Wales Branch, B.M.A.: Executive and Finance Committee.  
FEB. 13.—Tasmanian Branch, B.M.A.: Branch.  
FEB. 13.—Central Northern Medical Association, New South Wales: Clinical Meeting.  
FEB. 14.—Brisbane Hospital for Sick Children: Clinical Meeting.  
FEB. 19.—New South Wales Branch, B.M.A.: Medical Politics Committee; Organization and Science Committee.  
FEB. 19.—Illawarra Suburbs Medical Association, New South Wales.  
FEB. 20.—Victorian Branch, B.M.A.: Council.  
FEB. 22.—Queensland Branch, B.M.A.: Council.  
FEB. 28.—South Australian Branch, B.M.A.: Scientific Meeting.  
MAR. 5.—Victorian Branch, B.M.A.: Branch.  
MAR. 7.—Queensland Branch, B.M.A.: Branch.  
MAR. 12.—Tasmanian Branch, B.M.A.: Branch.

## Editorial Notices.

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